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(54) Title: GENETIC TYPING OF HUMAN GENES AND RELATED MATERIALS AND METHODS

(57) Abstract: Disclosed are novel polymorphisms in the human genes: CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDRI, LTF, MRP3, NR112, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5, nucleic acid molecules which include such polymorphisms and the methods of genotyping to identify the occurrence of such polymorphisms.

## GENETIC TYPING OF HUMAN GENES AND RELATED MATERIALS AND METHODS

### FIELD OF THE INVENTION

5           The present invention relates to the identification of various polymorphisms in different genes and methods and reagents for genotyping and phenotyping individuals using such polymorphisms.

### BACKGROUND OF THE INVENTION

10           Mutations in genes can result in over-production, altered function, or deficiency of a gene product. A polymorphism is a mutation that is inherited in a population (i.e., found in >1% of the population). If the affected gene product plays a key role in a biochemical pathway, such as metabolism or signaling, the result is often alteration of biological function that can cause disease, be associated with disease or an undesirable phenotype.

15           Diagnosis and treatment of a variety of disorders may often be accomplished through identification and/or manipulation of the genetic material which encodes for specific disease associated traits. In order to accomplish this, however, one must first identify a correlation between a particular gene and a particular trait. This is generally accomplished by providing a genetic linkage map through which one identifies a set of genetic markers that follow a particular  
20           trait. These markers can identify the location of the gene encoding for that trait within the genome, eventually leading to the identification of the gene. Once the gene is identified, methods of treating the disorder that result from that gene, i.e., as a result of overexpression, constitutive expression, mutation, underexpression, etc., can be more easily developed.

          One class of genetic markers includes polymorphic variations in the genetic code. In the  
25           course of evolution, the genome of a species can collect a number of variations in individual bases. Polymorphisms may exist as individual bases or as stretches of repeating sequences that vary as to the length of the repeat from individual to individual. Where these variations are recurring, e.g., exist in a significant percentage of a population, they can be readily used as markers linked to genes involved in mono- and polygenic traits. In the human genome, single-base  
30           polymorphisms occur roughly once per 300 bp. Indeed, polymorphic sequences are only useful as genetic linkage markers when the polymorphism can be detected separately from any other polymorphic sequence in the gene. Though many of these variant bases appear too infrequently among the allele population for use as genetic markers, useful polymorphisms (e.g., those occurring in 20 to 50% of the allele population) can be found approximately once per kilobase.  
35           Accordingly, in a human genome of approximately 3 Mb, one would expect to find approximately 3000 of these polymorphisms.

The use of polymorphisms as genetic linkage markers is thus of critical importance in locating, identifying and characterizing the genes which are responsible for specific traits. In particular, such mapping techniques allow for the identification of genes responsible for a variety of disease or disorder-related traits which may be used in the diagnosis and or eventual treatment of those disorders.

The human CYP1A1 gene is needed for the metabolism of polycyclic aromatic hydrocarbons. Its gene product, aromatic hydrocarbon hydroxylase, catalyzes the first step in the conversion of many compounds to carcinogenic forms. Jaiswal *et al.*, Science, 1985, vol. 228, pages 80-83 and Kawajiri *et al.*, Europ. J. Biochem. 1986, vol. 159, pages 219-225, isolated and analyzed the complete nucleotide sequence of a human genomic CYP1A1. Kawajiri *et al.* noted that the two sequences were nearly identical, with the exception of the two differences in the first intron which included an insertion of a 320 bp sequence and a deletion of a 650 bp sequence.

Seven polymorphisms have been described in the literature for the human CYP1A1 gene. Spurr *et al.*, Nucleic Acids Res. 1987, vol.15, page 5901 described the "m1" polymorphism, a T>C transition at position 3801 resulting in a MspI restriction fragment length polymorphism (RFLP) in the 3' noncoding region of the gene. The "m2" polymorphism was described by Hayashi *et al.*, J Biochem (Tokyo), 1991, vol. 110, pages 407-411, as an A>G transition in exon 7 (position 2455) that results in the substitution of a valine for isoleucine at codon 462. The authors associated the location of this polymorphism with the heme binding region of the protein. Crofts *et al.*, Carcinogenesis, 1993, vol. 9, pages 1729-1731, described a third variant commonly called "m3", that is a T>C transition in the 3' noncoding region of CYP1A1 (position 3205) and appears to be unique to African American populations. Cascorbi *et al.*, Cancer Res, 1996, vol. 56, pages 4965-4969, detected a 2453C>A transversion in exon 7 that results in a substitution of an asparagine for a threonine at codon 461. This variant has also been called "m4." Smart and Daly, Pharmacogenetics, 2000, vol. 10, pages 11-24, reported three polymorphisms in the human CYP1A1 gene. Two single nucleotide polymorphisms were identified in the 5' flanking region at positions -469 (C>T) and -459 (G>A) using a numbering system that assigns +1 to the transcription initiation site. Smart and Daly also reported a C>T transition in exon 3 at position 4151, again using +1 the initiation of transcription numbering, resulting in the substitution of arginine at codon 279 by tryptophan. The authors also reported finding a "highly polymorphic" region spanning -138 to -168 in the 5' flanking region that contained ten additional single-nucleotide polymorphisms in samples from eight individuals.

CYP1A2, a member of the cytochrome P450 superfamily, is a microsomal enzyme expressed in liver tissue. Ikeya *et al.*, Molec. Endocr., 1989, vol. 3, pages 1399-1408, identified the genomic sequence of the human CYP1A2 gene. The first exon, like that of CYP1A1, was found to be noncoding.

Several polymorphisms have been reported for the CYP1A2 gene. Nakajima *et al.*, Cancer Epidemiol. Biomarkers Prev., 1994, vol. 3, pages 413-421, found a silent mutation in exon 7, a T>C transition at position 5381. Nakajima *et al.*, J. Biochem. (Tokyo), 1999, vol. 125, pages 803-808, reported a -3858G>A transition in the 5' upstream region that resulted in decreased enzyme activity. Huang *et al.*, Drug Metab. Dispos., 1999, vol. 1, pages 98-101, identified a C>G single nucleotide polymorphism at position 63, resulting in the substitution of a leucine for phenylalanine at codon 21. Chida *et al.*, Jpn. J. Cancer Res. 1999, vol. 90, pages 899-902, identified three polymorphisms in the 5'-flanking region and intron 1 of human CYP1A2 in a Japanese population. They found a single nucleotide deletion at position -2464 (delT) and two single nucleotide polymorphisms, -740T>G and -164C>A. Sachse *et al.*, Br. J. Clin. Pharmacol. 1999, vol. 47, pages 445-449, found that the -164C>A mutation in intron 1 was associated with higher CYP1A2 inducibility in a group of Caucasian smokers.

The cytochrome P450 enzyme 2E1 is responsible for the metabolic activation of carcinogens and is also important in the metabolism of ethanol and acetaminophen. Song *et al.*, J. Biol. Chem. 1987, vol. 261, pages 16689-16697, isolated cDNA encoding a human ethanol-inducible P450. Umeno *et al.*, Biochemistry, 1988, vol. 27, pages 9006-9013, identified the genomic sequence of CYP2E1. Umeno *et al.* also identified a cDNA clone.

Brockmoller *et al.*, Cancer Res., 1996, vol. 56, pages 3915-3925, identified a C>G tranversion at position 9893 of a cDNA clone that contained the entire CYP2E1 amino acid coding region and 3' untranslated region. Hayashi *et al.*, J. Biochem. (Tokyo), 1991, vol. 110, pages 559-565, determined that a *Pst*I RFLP was localized to the single nucleotide polymorphism -1293 G>C and an *Rsa*I RFLP was identified as a C>T transition at position -1053. Hayashi *et al.* identified 3 additional single nucleotide polymorphisms linked to the *Rsa*I RFLP at -1165G>A, -991T>C, and -771T>C from transcription start, corresponding to approximate positions of -1199, -1025, and -805 using the nomenclature of Antonarakis, Hum. Mutat., 1998, vol. 11, pages 1-3. Persson *et al.*, FEBS Lett., 1993, vol. 319, pages 207-211, examined a Swedish population for genetic polymorphism in the CYP2E1 gene. These authors detected a *Dra*I RFLP in exon 6. This polymorphism has been assigned as a 7632T>A (*CYP allele website*), 7766A>T (Persson *et al.*), or 7666A>T tranversion (Brockmoller *et al.*).

Hu *et al.*, Mol. Pharmacol., 1997, vol. 51, pages 370-376, described two variants in the coding region of the gene. A G>A transition in exon 2 (position 1132) resulted in the replacement of arginine at codon 76 by histidine and was found to have reduced activity *in vitro*. A G>A transition in exon 8, position 10023, resulted in the replacement of valine at codon 389 by isoleucine, but appeared to have the same activity as wildtype CYP2E1 protein. Fairbrother *et al.*, Pharmacogenetics, 1998, vol. 8, pages 543-552, examined DNA from 40 healthy unrelated Caucasians and detected 6 novel single nucleotide polymorphisms by single strand conformational



polymorphism analysis. They detected three polymorphisms in the 5' upstream region, -316A>G, -297T>A, and -35G>T from the transcription start site, as well as a G>C tranversion in intron 1, position 1107 relative to the transcription start. The authors also reported a G>A transition in exon 4, position 4768, resulting in a substitution of isoleucine for valine at codon 179 and a silent mutation in exon 8, 10157C>T relative to the transcription start site.

Hu *et al.*, Biochem. Biophys. Res. Commun., 1999, vol. 263, pages 286-293, identified individuals with differing tandem repeats of 42 to 60 bases in length resulting in a *Xba*I RFLP in the 5' flanking region. The genomic DNA published by Umena *et al.*, had only 5 of these repeats. Fritsche *et al.*, Mutat. Res., 2000, vol. 432, pages 1-5, sequenced a polymorphism in the 5' flanking region that consisted of a 90 base insertion of 2 identical repeats at position -2029 and a 6 base insertion at position -2071 relative to transcription start. The authors also detected a C>T transition at position -2245 relative to the transcription start site in all individuals who possessed the 96 base insertion polymorphism.

Nomenclature and numbering of polymorphisms for CYP2E1 mutants vary according to author. The table below outlines some of the different nomenclature and nucleotide position assignments for CYP2E1 polymorphisms reported in the literature. Unless otherwise specified, all nomenclature in the text above follows the recommendations of the Nomenclature Working Group as reported in Antonarakis, *supra*. Using the Working Group recommendations, the base A in the initiation codon ATG is denoted as +1 and the base before A is numbered -1. In other references, +1 numbering starts at the putative transcription initiation site.

**Table 1: Summary of Single Nucleotide Polymorphisms for CYP2E1:**

Nucleotide position assigned by:					
CYP Allele	CYP	RFLP Mutant			
Assignment	Nomenclature	Authors	Common Name	Reference	
25 *1B	9893C>G	9930C>G	TaqI- A1=TaqI- /A2=TaqI+	Brockmoller <i>et al</i>	
*2	1132G>A	1168G>A		Hu <i>et al</i> (1997)	
*3	10023G>A	10059G>A		Hu <i>et al</i> (1997)	
30 *4	4768G>A	4804G>A		Fairbrother <i>et al</i>	
*5A, *5B	-1293G>C	-1259G>C	PstI+ c1=PstI-/c2=PstI+	Hayashi <i>et al</i>	
35 *5A, *5B	-1053C>T	-1019C>T	RsaI- c1=RSA+/c2=Rsa-	Hayashi <i>et al</i>	
*5A, *6	7632T>A	7766A>T or 7666A>T	DraI- C=DraI-/D=DraI+	Persson <i>et al</i> Brockmoller <i>et al</i>	

	*7A, *7B, *7C	261T>A	-297T>A	Fairbrother <i>et al</i>
	*7B	-71G>T	-35G>T	Fairbrother <i>et al</i>
5	*7C	280G>A	-316G>A	Fairbrother <i>et al</i>
	none		1107G>C	Fairbrother <i>et al</i>
10	none		10157C>T	Fairbrother <i>et al</i>
	none		-1165G>A	Hayashi <i>et al</i>
	none		-991T>C	Hayashi <i>et al</i>
15	none		-771T>C	Hayashi <i>et al</i>
	none		-2245C>T	Fritsche <i>et al</i>

20

**Table 2: Summary of Insertion Polymorphisms for CYP2E1**

CYP			
	Allele	Polymorphism	Reference
25	*1A (wildtype)	5 repeats in 5' flanking region	Umeno <i>et al</i>
	*1C	6 repeats in 5' flanking region	Hu <i>et al</i> (1999)
30	*1D	8 repeats in 5' flanking region	Hu <i>et al</i> (1999)
	*1D?	90 bp insertion at -2029 and 6 bp insertion at -2071	Fritsche <i>et al</i>
35			

The gene product of the ADRB1 gene, the beta-1 adrenergic receptor, is an important cell surface signaling protein which belongs to a family of receptors that are coupled to guanine nucleotide binding regulatory proteins (G proteins). Frielle *et al.*, Proc. Nat. Acad. Sci., 1987, vol.

84, pages 7920-7924, cloned the ADBR1 gene from a human placental cDNA library and determined its sequence.

One RFLP and two single nucleotide polymorphisms (SNPs) in the human ADBR1 gene have been reported in the literature. Berrettini and Hoehe, *Nucleic Acids. Res.*, 1988, vol. 16, page 7754, detected a biallelic RFLP using Bgl I, yielding 6.2 kb and 4.7 kb fragments. The exact location of this RFLP is not known. Mason *et al.*, *J. Biol. Chem.*, vol. 274, pages 12670-12674 and Tesson *et al.*, *J. Mol. Cell. Cardiol.*, 1999, vol. 31, pages 1025-1032 reported detecting a G>C polymorphism at position 1165, resulting in the substitution of arginine for glycine at amino acid position 389. Mason *et al.* also reported that the location of 1165C>G polymorphism corresponds to a G-protein coupling domain in the protein, and found that the Arg-389 variant receptor displayed enhanced adenylyl cyclase activation relative to the Gly-389 variant. Maqbool *et al.*, *Lancet*, 1999, vol. 353, page 897 and Moore *et al.*, *Hum. Mutat. (Online)*, 1999, vol. 14, page 271, detected a single nucleotide polymorphism, 145A>G, which results in the substitution of glycine for serine at amino acid 49 in the extracellular amino-terminal region of the receptor.

The aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor that regulates multiple genes inducible by environmental pollutants such as dioxins (TCDD), aromatic hydrocarbons, and halogenated biphenyls. After binding a ligand such as dioxan, the aryl hydrocarbon receptor activates the transcription of a number of genes encoding drug-metabolizing enzymes, including the cytochromes P450 1A1 and 1A2. Dolwick *et al.*, *Mol. Pharmacol.*, 1993, vol. 44, pages 911-917, cloned and expressed a cDNA for human AHR using mouse cDNA to probe a human hepatoma cDNA library. Ema *et al.*, *J. Biochem. (Tokyo)*, 1994, vol. 116, pages 845-851, isolated a human cDNA for the AHR gene having a sequence identical to that reported by Dolwick *et al.* Micka *et al.*, *Pharmacogenetics*, 1997, vol. 7, pages 95-101, sequenced 93 nucleotides of AHR exon 9 in five individuals and determined that human AHR does not contain a functional polymorphism analogous to one found in that region of the mouse AHR gene, an alanine to valine at mouse codon 375. Eguchi *et al.*, *Biochem Biophys Res. Commun.*, 1994, vol. 203, pages 615-622, cloned the promoter region of the AHR gene from a human placental genomic library and reported the sequence from -812 to the initiation of translation site. Hayashi *et al.*, *Carcinogenesis*, 1994, vol.15, pages 801-806 isolated genomic clones of the human AHR gene from a human placental library and partially determined their sequence.

Several polymorphisms have been reported for the human AHR gene. Jones *et al.*, *Hum. Mol. Genet.*, 1994, vol. 3, page 2083, reported a *MspI* RFLP for the human AHR gene in which a polymorphic 2.7 kb fragment was detected with a frequency of 0.63 in 27 unrelated Caucasians. The authors designated the 2.7 kb fragment as allele "A1," and its absence as "A2." An additional *MspI* fragment of 2.2 kb was detected in 2 of the 27 individuals. The nucleotide changes resulting

in these RFLPs were not identified. Itoh and Kamataki, Nucl. Acids. Res., 1993, vol. 21, page 3578, isolated a human AHR cDNA from a human HepG2 cell line that contained a frameshift mutation due to the insertion of an additional thymine in a cluster of 4 thymines at nucleotides 2498 to 2501. Using single-strand conformational polymorphism (SSCP) analysis, Kawajiri *et al.*,  
5 Pharmacogenetics, 1995, vol. 5, pages 151-158, detected two types of variants in a group of Japanese individuals. One was a silent mutation (an AAT to AAC) located at codon 44 in exon 2. The second was a 554A>G in exon 10, resulting in the replacement of arginine (AGA) by lysine (AAA) at codon 554. Wanner *et al.*, Pharmacogenetics, 1999, vol. 9, pages 777-780, also detected the codon 554 polymorphism in a group of Caucasians. Smart and Daly, Pharmacogenetics, 2000,  
10 vol. 10, pages 11-24, performed SSCP analysis of the exons of the AHR gene using DNA samples from healthy Caucasian and African Americans and identified the codon 554 mutation as a G>A substitution at position 1721. In addition, the authors identified a novel polymorphism at codon 570, resulting in the substitution of valine by isoleucine. The authors identified the nucleotide change as a G>A substitution at position 1768.

15 The cytosolic dioxin receptor translocates to the nucleus upon binding of a ligand. Ligands for the receptor include dioxin and other polycyclic aromatic hydrocarbons. The receptor-ligand complex then increases transcription of multiple genes involved in the metabolism of polycyclic aromatic hydrocarbon procarcinogens. The aryl hydrocarbon receptor nuclear translocator (ARNT) gene encodes a protein that is the component of the receptor required for  
20 translocation to the nucleus. Using a panel of mouse/human somatic cell hybrids, the authors localized the human gene to 1pter-q12. Hoffman *et al.*, Science, 1991, vol. 252, page 954-958, isolated a portion of the ARNT genomic sequence by searching for human genes that complemented mouse hepatoma cells defective in AHR nuclear translocation.

Several polymorphisms have been reported for the human ARNT gene. Johnson *et al.*,  
25 Hum. Mol. Genet., 1992, vol. 1, page 351, found that hybridizing human *MspI*-digested DNA with a labeled ARNT cDNA probe identified two polymorphic alleles with fragments of 2.80 kb (A1) and 2.67 kb (A2). In a group of 41 unrelated Caucasians, the frequency of the A1 and A2 alleles were 0.62 and 0.38, respectively. Wilson *et al.*, Arch. Biochem. Biophys., 1997, vol. 346, pages 65-73, detected a variant of ARNT in a human breast cancer cell line that resulted in a truncated  
30 protein of only 325 amino acids. The variant was shown to be the result of a deletion from nucleotides 1038 to 2322 that generated a premature translational stop codon. Cao and Hegele, J. Hum. Genet., 2000, vol. 45, pages 92-93, detected a novel A>C change in exon 16 of the human ARNT gene, predicting the substitution of an asparagine (AAC) for an aspartate (GAC) at codon 511.

35 The human cathepsin S (CTSS) gene codes for an elastinolytic cysteine protease belonging to the papain superfamily. Cathepsin S is involved in physiological protein degradation

and is believed to be important in pathological tissue destruction and invasion, immunity and atherosclerosis, and spleen, heart, and lung tissues, and at sites of arterial wall matrix remodeling.

Shi *et al.*, J. Biol. Chem., 1992, vol. 267, pages 7258-7262, isolated a 1.7 kb full-length CTSS cDNA from a human alveolar macrophage cDNA expression library. Wiederanders *et al.*,  
5 J. Biol. Chem., 1992, vol. 267, pages 13708-13713, isolated a full-length CTSS cDNA. Shi *et al.*, J. Biol. Chem., 1994, vol. 269, pages 11530-11536, characterized exons 1 through 5, introns 1 through 4 and part of intron 5, and more than 7kb of the 5' flanking sequence of the CTSS genomic gene.

One polymorphism has been reported to date in the literature for the human CTSS gene.  
10 Cao and Hegele, J. Hum. Genet., 2000, vol. 45, pages 94-95, identified a single nucleotide polymorphism within exon 1 in the promoter region, -25G>A, which could be detected with the restriction endonuclease Bfml.

Leukotrienes are biologically active arachidonic acid metabolites which have been implicated in a variety of inflammatory responses, including asthma, arthritis and psoriasis.  
15 Dixon *et al.*, Nature, 1990, vol. 343, pages 282-284, isolated a human cDNA encoding the gene for 5-lipoxygenase-activating protein (FLAP) and demonstrated that the protein is necessary for leukotriene synthesis in intact cells. Kennedy *et al.*, J. Biol. Chem., 1991, vol. 266, pages 8511-8516, found that the human FLAP gene consists of 5 small exons and four large introns, and spans more than 31 kb. The authors identified a RFLP in the second intron of the gene, a T>C transition  
20 resulting in a new *Hind*III site, thus correcting the FLAP sequence reported by Dixon *et al.* Yandava *et al.*, Genomics, 1999, vol. 56, pages 131-133, mapped the FLAP gene to 13q12 by analysis of radiation hybrids, inclusion in mapped clones, and by *in situ* hybridization. They noted that this localization was outside the asthma susceptibility region on chromosome 13.

Methylation is an important pathway in the biotransformation of many drugs,  
25 neurotransmitters, and xenobiotic compounds. Histamine N-methyltransferase (HNMT) catalyzes a major pathway in histamine metabolism via N(tau)-methylation, and it also methylates compounds structurally related to histamine. Histamine has a wide range of physiological actions: it plays important roles in allergy, anaphylaxis, the regulation of gastrointestinal acid secretion, and neurotransmission in the brain. There is wide variation in the levels of HNMT activity among  
30 humans, which has been shown to be primarily due to the effects of inheritance. Girard *et al.*, Mol. Pharmacol., 1994, vol. 45, pages 461-468 and Yamauchi *et al.*, Am. J. Physiol., 1994, vol. 267, pages L342-349, cloned and expressed human kidney HNMT cDNAs. Both groups identified a 1.4kb clone containing the full 876 nucleotide reading frame coding for a 292 amino acid protein having approximately 83% homology to the rat kidney HNMT. Aksoy *et al.*,  
35 Biochem. Biophys. Res. Commun., 1996, vol. 219, pages 548-554, determined the genomic structure of the human HNMT gene and localized it to chromosome 2.

Several variants have been reported for the human HNMT gene. Aksoy *et al.*, *supra*, identified two single nucleotide variants reported for the published human HNMT cDNA sequences: C or T at position 314 (codon 105), and A or G at position 595 (codon 199). Preuss *et al.*, Mol. Pharmacol., 1998, vol. 53, pages 708-717, analyzed DNA from a total of 114 human renal biopsy samples obtained from Caucasian patients. The authors detected two single nucleotide polymorphisms, a C>T transition at nucleotide 314 in exon 4 and an A>G transition at nucleotide 939 within the 3' untranslated region. The C>T transition, C314T polymorphism, resulted in an amino acid substitution of isoleucine (Ile) for threonine (Thr) at position 105, and the less common Ile-105 allele was associated with decreased levels of HNMT activity. Yan *et al.*, Pharmacogenetics, 2000, vol. 10, pages 261-266, reported an association between the human HNMT gene C314T (Thr105Ile) variant and asthma. They found that the Ile-105 variant was more common in a group of 192 Caucasian asthma patients compared to 237 Caucasian controls.

Human glandular kallikrein (KLK2) is a member of the kallikrein family of genes, a subfamily of serine proteases. Schedlich *et al.*, DNA, 1987, vol. 6, pages 429-437, described the sequence of a human glandular preprokallikrein genomic gene, that they called hGK-1 which is an alternative name for KLK2, isolated from a human genomic library.

Several RFLPs have been reported for the human KLK2 gene. Hermens *et al.*, Nucleic Acids. Res., 1990, vol. 18, page 208, examined ten individuals and detected a biallelic *MspI* RFLP (1.8 kb / 2.0 kb) in the human KLK2 gene. Riegman *et al.*, Genomics, 1992, vol. 14, pages 6-11, identified one *TaqI* RFLP (2.5 kb to 5.0 kb) and one *MspI* RFLP (an additional 0.6 kb fragment) in a group of thirty-one individuals. The nucleotide changes resulting in these RFLPs were not identified. Herrala *et al.*, Clin. Chem., 1997, vol. 43, pages 279-284, described a single nucleotide polymorphism in the human KLK2 gene, a C to T change at position 792, resulting in the substitution of tryptophan (Trp) for arginine (Arg) at codon 226. They reported that recombinant KLK2 protein containing Arg226 was an active protein but that the Trp226-containing recombinant KLK2 was inactive.

The quinone oxidoreductases NQO1 and NQO2 are cytosolic flavoproteins that catalyze the metabolic detoxification of quinones and their derivatives, leading to the protection of cells against redox cycling and oxidative stress. The NQO2 gene codes for a form of quinone oxidoreductase which requires dihydronicotinamide riboside (NRH) as a cofactor, and thus the protein is also sometimes referred to as NRH:quinone oxidoreductase 2.

Jaiswal *et al.*, Biochemistry, 1990, vol. 29, pages 1899-1906, screened a human liver cDNA library by hybridization with a NQO1 gene cDNA probe and isolated a cDNA for the NQO2 gene. Jaiswal, J. Biol. Chem., 1994, vol. 269, pages 14502-14508, characterized the gene structure of NQO2, including 1336 bp of the 5' flanking region and 165 bp of the 3' flanking

region. He estimated the length of the gene to be approximately 20 kb, composed of seven exons and six introns, with the first exon noncoding.

The NQO2 gene showed extensive polymorphism by RFLP analysis. Jaiswal *et al.*, Pharmacogenetics, 1999, vol. 9, pages 413-418, used the restriction enzymes *EcoRI*, *HindIII*,  
5 *BamHI*, *EcoRV*, *XbaI*, *SacI*, *BglII*, *PstI*, *KpnI*, *TaqI*, *PvuII*, and *MspI* to examine 29 human peripheral leukocyte DNA samples for polymorphism in the NQO2 gene. Three NQO2 probe fragments were created by digestion with *BamHI* and *PstI*, a 233- bp *EcoRI*-*BamHI* 5' fragment, a 580- bp *BamHI*-*PstI* middle fragment, and a 166- bp *PstI*-*EcoRI* 3' fragment. RFLPs localized to the 5', middle, or 3' regions of the gene were detected using these probes with seven of the  
10 restriction enzymes tested. Digestion of genomic DNA with *EcoRI*, *PstI*, and *PvuII* enzymes showed RFLPs only with the 5' probe. Both the middle and 3' probes detected RFLPs with genomic DNA digested with *EcoRV*, *SacI*, *BglII*, *TaqI*, and *MspI*. All three probes detected RFLPs with *SacI*, *TaqI*, and *MspI*. The specific polymorphic nucleotide sequences corresponding to these RFLPs were not reported by the authors.

15 Methylation is an important metabolic pathway in the biotransformation of many clinically useful drugs and xenobiotic compounds. The gene product of the nicotinamide N-methyl transferase (NNMT) gene catalyzes the S-adenosyl methionine-dependent N-methylation of nicotinamide and other pyridines to form pyridinium ions. Aksoy *et al.*, J. Biol. Chem., 1994, vol. 269, pages 14835-14840, isolated a human liver NNMT cDNA of 969 bases with an open  
20 reading frame of 792 bases encoding a 264- amino acid protein. Aksoy *et al.*, Genomics, vol. 29, pages 555-561, isolated a cosmid clone from a chromosome 11-specific genomic library and used it to characterize the NNMT gene. The authors reported the NNMT gene to be approximately 16.5 kilobases long comprising 3 exons and 2 introns, and identified a site of transcription initiation 105 to 109 bp upstream of the translation initiation codon. Yan *et al.*,  
25 Pharmacogenetics, 1999, vol. 9, pages 307-316, isolated DNA from 27 human liver biopsy samples with either low, intermediate, or high levels of NNMT activity. They amplified the three exons, 1240 nucleotides of intron 1 and approximately 700 nucleotides of the 5'-flanking region of the NNMT gene from each of these samples with the polymerase chain reaction, and then sequenced the amplified DNA to identify genetic polymorphisms that might correlate with NNMT  
30 phenotype. No SNPs or insertion/deletion events were detected within the exons or 5'-flanking regions of NNMT. The authors reported finding eight SNPs within intron 1, although none appeared to be related to the level of NNMT activity. The SNPs detected were G34C, T44C, C83G, G402T, C507G, G567A, T621C and T1025C, numbered from 5' to 3' within the intron. The authors concluded that polymorphisms within the exons and 5'-flanking region of the NNMT  
35 gene are unlikely to be related to wide individual variations in the level of this enzyme activity in the human liver.

Sulfotransferases transfer a sulfate group from a cofactor, 3'phosphoadenosine-5'-phosphosulfate, to hydroxyl, amino, sulfhydryl, or N-oxide groups on their substrates. Cytosolic forms of these enzymes metabolize xenobiotics and endogenous compounds such as hormones and neurotransmitters, and are widely expressed in human tissues. Sulfotransferases have been  
5 classified into two subfamilies, SULT1 and SULT2, on the basis of their substrate specificity and amino acid sequence. The enzyme encoded by the gene for STM, a thermolabile form of sulfotransferase, preferentially sulfates dopamine and other endogenous catecholamines. It shares 93% sequence homology with the gene product of SULT1A1, the thermostable or phenol-sulfating sulfotransferase. Other names for STM include STM (monoamine-preferring sulfotransferase),  
10 TL-PST (thermolabile phenol sulfotranferase), M-PST (catecholamine-sulfating phenol sulfotransferase), ST1A5, and HAST3 (human aryl sulfotransferase 3).

STM cDNAs have been cloned from several human tissues. Zhu *et al.*, Biochem. Biophys. Res. Commun., 1993, vol. 195, pages 120-127, cloned a 1424 bp full-length STM cDNA (which they called HAST3) from a human brain library. Human STM cDNAs with identical open  
15 reading frames were isolated by Wood *et al.*, Biochem. Biophys. Res. Commun., 1994, vol. 198, pages 1119-1127, from human liver and by Jones *et al.*, Biochem. Biophys. Res. Commun., 1995, vol. 208, 855-862, from human platelets. Using a total human genomic library, Aksoy and Weinshilboum, Biochem. Biophys. Res. Commun., 1995, vol. 208, pages 786-795, cloned and characterized the STM gene, including 0.6 kb of 5' flanking and 0.4 kb of 3' flanking sequences.  
20 They reported the STM gene was approximately 8.4 kb in length and consisted of 10 exons and 9 introns, of which the exons 1 through 3 and parts of exons 9 and 10 were noncoding. The amino acid-encoding portion of the gene was identical in sequence to the open reading frames reported for the STM cDNAs.

Plasminogen activators are proteases that activate plasminogen to plasmin. Plasminogen  
25 activation has been implicated in fibrinolysis as well as in tissue remodeling, cell migration and tumor metastasis. At least two types of plasminogen activators have been identified in humans. Urokinase, also known as u-PA or uPA, is the urinary plasminogen activator and t-PA, also called PLAT, is the tissue plasminogen activator. Both have been used clinically for thrombolytic disorders.

30 Nagai *et al.*, Gene, 1985, vol. 36, pages 183-188, cloned a cDNA for preprourokinase from human kidney cells. The authors indicated that codons 1 to 157 and 159 to 411 encoded the A and B chains, respectively, and the lysine linking the two peptides at codon 158 would be proteolytically removed. Nagai *et al.* noted a number of differences between their cDNA sequences and partial sequence reported by Verde *et al.*, Proc. Natl. Acad. Sci. U S A, 1984, vol.  
35 81, pages 4727-4731, and Heyneker *et al.*, European Patent Application No. 83103629.8. Compared to Verde *et al.*, Nagai *et al.* documented one nucleotide difference (ATC vs. ATG) that



coded for leucine rather than methionine at codon 194. Nagai, *et al.* also identified codon changes that resulted in four silent changes: AAG to AAA (Lys3), CTG to CTA (Leu340), CCA to CCC (Pro345), and CAG to CAA (Gln346) when compared with Verde *et al.* With respect to differences with the Heyneker *et al.* sequence, Nagai *et al.* indicated that the 5'-untranslated region was four nucleotides longer than the sequence reported by Heyneker, *et al.* In particular, the GGCC at position -34 to -31 and the G at position -42 upstream from ATG are absent from the Heyneker, *et al.* sequence and the GC at positions -58 and -57 upstream from the ATG were deleted from the Hayneker *et al.* sequence. The codons CTG for Leu 340, CCA for Pro 345 and CAG for Gln 346 were substituted by CTA, CCC and CAA, respectively, in the Heyneker *et al.* sequence.

Riccio *et al.*, Nucleic Acids Res., 1985, vol. 13, pages 2759-2771, isolated and characterized the human uPA gene and its promoter. The gene spanned 6.4 kb and consisted of 11 exons separated by 10 introns. The authors also compared the sequences of the gene with the cDNA sequences of Verde *et al.* and Heyneker *et al.*, and identified several silent base substitutions in the coding sequence as well as several changes, additions and deletions in the 3' flanking region.

Sebastio *et al.*, Nucleic Acids Res., 1985, vol. 13, page 5404, identified a biallelic polymorphism yielding a common 7.0 kb fragment and less frequent 1.6 kb fragment using the restriction enzyme *Bam*HI. Conne *et al.*, Thromb. Haemost., 1997, vol. 77, 434-435, examined human DNA samples for polymorphism in exons 3 through 8 of the human uPA gene using SSCP analysis. The authors detected a C>T polymorphism at nucleotide 2206 (relative to +1 at the transcription start site), resulting in the substitution of a proline for a leucine at codon 121 in exon 6. The authors detected a T>C polymorphism at nucleotide 2836 in the intron near the beginning of exon 8. Conne *et al.*, Thromb. Haemost., 1997, vol. 78, page 973, noted that although two different amino acid sequences had been reported for human uPA in the EMBL database (SWISS PROT, AN:P00749), either methionine or isoleucine at codon 194 in exon 7, only the isoleucine codon (2583C) was detected in the more than 200 alleles they tested.

The following references describe certain genetic discoveries related to the human muscarinic receptor genes CHMR1, CHMR2, CHMR3, CHMR4, and CHMR5. Molecular cloning studies have revealed the existence of five distinct human muscarinic acetylcholine receptors m1-m5 (HUGO names: CHMR 1 – CHMR5), which differ in their tissue distribution, ligand binding properties, and functional profiles. Structurally and functionally, the muscarinic receptors are members of the superfamily of G protein-coupled receptors and mediate many of the actions of the neurotransmitter acetylcholine in the central and peripheral nervous systems.

Bonner *et al.*, Science, 1987, vol. 237, pages 527-532, cloned and expressed the genes for the human muscarinic acetylcholine receptors CHMR1, CHMR2, CHMR3, and CHMR4, and

reported their genomic sequences. Peralta *et al.*, EMBO. J., 1987, vol. 6, pages 3923-3929, published amino acid sequences, tissue expression and binding properties for these four genes. Bonner *et al.*, Neuron, 1988, vol.1, pages 403-410, cloned a fifth muscarinic receptor, CHMR5. One single nucleotide polymorphism (SNP) has been described for the CHMR1 gene and one RFLP for the CHMR4 gene. Ohara *et al.*, Neurosci. Lett., 1994, vol. 178, pages 23-26, examined postmortem brain samples from a group of 18 individuals in Japan (9 Alzheimer patients, 6 vascular dementia patients and 3 controls) for polymorphisms in the CHMR1 and CHMR2 genes. They detected a G to A nucleotide change at position 616 in the CHMR1 gene in samples from 2 individuals (1 Alzheimer and 1 vascular dementia patient). The resulting ACG to AGA codon change does not alter the coded amino acid, threonine. They detected no polymorphisms in the CHMR2 gene. Detera-Wadleigh *et al.*, Nucleic Acids Res., 1989, vol. 17, page 6431, identified a SstI polymorphism in the CHMR4 gene in a study of 19 unrelated North Americans. SstI identified two allelic fragments of 3.5kb and 3.2 kb, with frequencies of 0.1 and 0.9, respectively. No genetic polymorphisms have been reported in the literature for CHMR2, CHMR3 or CHMR5.

Diazepam binding inhibitor (DBI) is a polypeptide of approximately 10 kD that is expressed in a variety of human tissues and organs. DBI is believed to be active in many different biological processes, including steroidogenesis and peptide hormone release. It has since been identified independently as acyl-CoA-binding protein (ACBP) based on its ability to bind and induce the synthesis of acyl-Co-A esters.

Gray *et al.*, Proc. Natl. Acad. Sci. USA, 1986, vol. 83, pages 7547-7551, isolated a cDNA clone encoding human DBI from hypothalamus and liver cDNA libraries. The authors also reported the existence of multiple genes coding for DBI and suggested that one or more might be pseudogenes. Webb *et al.*, DNA, 1987, vol. 6, pages 71-79, cloned a cDNA for an endogenous ligand for the GABA-A receptor, which they called endozepine. The cDNA was 405 bases in length, with 57 and 87 bases of noncoding 5' and 3' sequences, respectively. Kolmer *et al.*, Biochem. J., 1995, vol. 306, pages 327-330 cloned two different cDNAs corresponding to RNA transcripts of two different sizes, 237 and 287 nucleotides. Swinnen *et al.*, DNA Cell. Biol., 1996, vol. 15, pages 197-208, cloned and characterized a human DBI gene and its promoter region. The gene consisted of 5 exons separated by 4 introns, and included approximately 1.2 kb of sequences upstream of a putative transcription initiation site. Gersuk *et al.*, Genomics, 1995, vol. 25, pages 469-476, cloned and sequenced a pseudogene of DBI.

Epoxide hydrolases add water to epoxides to form the corresponding diol. Cytosolic epoxide hydrolase acts to detoxify a variety of mutagenic, carcinogenic and toxic xenobiotic epoxides, and is also involved in the metabolism of arachidonic and linoleic acid epoxides. Beetham *et al.*, Arch. Biochem. Biophys., 1993, vol. 305, pages 197-201, isolated and sequenced EPHX22 cDNA from a human liver library. The 2110- nucleotide clone contained a coding

region of 1662 nucleotides. Sandberg and Meijer, *Biochem. Biophys. Res. Commun.*, 1996, vol. 221, no. 333-339, isolated and characterized a series of EPHX2 genomic clones from a human placental genomic library. The authors determined that the EPHX2 gene was approximately 45 kb long, contained 19 exons, and predicted a 555 amino acid protein. In addition, they noted several differences from the previously reported cDNA sequence of Beetham *et al.* Two nucleotide differences were detected in exon 1, causing a substitution of alanine for glycine at codon 5. The authors suggested the conserved substitution was likely to be a genetic polymorphism. In exon 7, three extra nucleotides resulting in a short frame-shift were identified, changing a methionine to a serine and adding a new glycine. In addition, two new bases were introduced while one base was not found in the 3' flanking region of the EPHX2 gene compared to the published cDNA sequence.

Lactotransferrin, also known as lactoferrin or LTF, is a member of a family of iron-binding proteins that modulate iron metabolism, hemopoiesis and immunologic reactions. LTF was first discovered in milk, but is found in other biological fluids and tissues. Several authors have published sequence data for human lactoferrin cDNAs. Rado *et al.*, *Blood*, 1987, vol. 70, pages 989-993, cloned and sequenced a partial lactotransferrin cDNA from a human neutrophil library. Powell and Ogden, *Nucleic Acids Res.*, 1990, vol. 18, page 4013, isolated a lactotransferrin cDNA from human breast tissue and reported sequence data for the entire mature protein as well as 17 amino acids of a putative signal peptide. Rey *et al.*, *Nucleic Acids Res.*, 1990, vol. 18, page 5288, isolated and sequenced a full-length human mammary gland LTF cDNA. Tweedie *et al.*, *Adv. Exp. Med. Biol.*, 1994, vol. 357, pages 197-208, isolated a full-length cDNA for the human lactoferrin gene from human bone marrow and expressed the gene in baby hamster kidney (BHK) cells. Panella *et al.*, *Cancer Res.*, 1991, vol. 51, pages 3037-3043, isolated a lactoferrin cDNA from a normal human breast tissue library and summarized the differences between their LTF sequence and those of the previously published LTF cDNAs. The cDNA isolated by Panella *et al.* contained an extra cytosine at nucleotide 2097, corresponding to codon 699, causing a frameshift at the 3' end. Compared to the cDNA of Rado *et al.*, the sequence of Panella *et al.* predicted a glycine rather than an alanine at codon 486, GGC to GCG at nucleotides 1456-1458, and also possessed two silent base differences. The human breast tissue cDNA of Rey *et al.* differed at codon 147, ATA>ATC, predicting an isoleucine instead of threonine and codon 421, GGC>GTC, predicting a glycine rather than cysteine. One silent base difference was also detected. Teng, *Adv. Exp. Med. Biol.*, 1994, vol. 357, pages 183-196, isolated and characterized the LTF promoter and 5'-flanking sequences from human and mouse. The complete gene encoding human lactoferrin was isolated by Kim *et al.*, *Mol. Cells*, 1998, vol. 8, pages 663-668, from a human placental cosmid library, and its structure was characterized. The authors estimated the length of the gene to be 24.5 kb, consisting of 17 exons separated by introns of 300bp - 3.3 kb.

Panella *et al.* performed Southern analysis of DNA from normal leukocytes, leukemic cells and breast cancer cells using their human LTF cDNA as a probe, and found that the human lactoferrin gene was polymorphic when tested with the restriction enzymes *MspI* and *XbaI*. Penco *et al.*, Cancer Biochem Biophys, 1999, vol. 17, pages 163-178, analyzed the lactoferrin promoter  
5 region from patients with sporadic breast cancer and found one polymorphic site by SSCP analysis, a C>T change at nucleotide -418. (Note: The numbering convention was not identified, but is believed to be from the transcription initiation site).

Arachidonic acid metabolites mediate inflammation and thrombosis. The enzyme responsible for the committed step in the biosynthesis of prostaglandins and thromboxane from  
10 arachidonic acid is cyclooxygenase (COX), also known as prostaglandin-endoperoxide synthase. Two isoforms of COX2, both expressed in cells involved in inflammatory processes, have been identified: a constitutively expressed COX1, and a mitogen-inducible form, COX2. Hla and Neilson, Proc. Nat. Acad. Sci. U.S.A., 1992; vol. 89, pages 7384-7388, cloned and expressed a human COX2 cDNA from human umbilical vein endothelial cells. Jones *et al.*, J. Biol. Chem.,  
15 1993, vol. 268, pages 9049-9054, isolated a human COX2 cDNA from an endothelial cell cDNA library. The authors detected a RFLP in DNA samples from four of 78 individuals tested with the restriction enzyme *HindIII*, and concluded that COX2 was polymorphic.

Kosaka *et al.*, Eur. J. Biochem, 1994, vol. 221, pages 889-897, isolated a human genomic COX22 clone that was 8.3 kb long, consisting of 10 exons and 1.69 kb of 5' flanking region. The  
20 authors reported that their clone showed 2 nucleotide differences in the coding region compared to the published sequence of Hla and Neilson, *ibid*. A guanine was detected at position 2916 in exon 5 that resulted in a predicted amino acid change to glycine, and a silent nucleotide change to an adenine was identified at position 4150 in exon 7. Kosaka *et al.* also found that the 3' untranslated region contained 45 nucleotide differences over a span of 1870 bases. Tazawa *et al.*,  
25 Biochem. Biophys. Res. Commun., 1994, vol. 203, pages 190-199, also isolated the entire PGHS2 genomic gene and 1.8 kb of 5' flanking region. They found that that the gene contained 10 exons and was approximately 7.5 kb long. Appleby *et al.*, Biochem. J., 1994, vol. 302, pages 723-727), reported the structure of the human COX22 gene. They isolated genomic DNA sequences beginning 0.8 kb upstream of the transcription start site and spanning 6 kb of the coding region  
30 (encompassing 10 exons separated by 9 introns), as well as 2.5 kb of the 3'-UTR.

Certain investigators have identified COX22 gene polymorphisms. Humar *et al.*, Int. J. Cancer, 2000, vol. 87, pages 812-817, performed SSCP analysis on samples from 130 members of a familial adenomatous polyposis (FAP) family displaying strong phenotype variation. The authors identified three polymorphic sites within the coding region and two polymorphic sites  
35 within the promoter of the COX22 gene. In the coding region, the two identified polymorphisms were silent changes, one at position 2191 (GTC > GTG) in exon 3 and the other at position 6698

(GGT > GGG) in exon 10. A third polymorphism was identified as a "double sequence" from nucleotides 4534 to 4789 in exon 7. Two polymorphisms were also detected within the COX22 promoter at positions -899 and -197, both G to C changes. Spirio *et al.*, Cancer Res., 1998, vol. 58, pages 4909-4912, had examined the COX22 gene from 56 patients with attenuated FAP. The authors used PCR sequence analysis to examine the entire coding region, the 3'-UTR in exon 10, and the first 1000 bp of the promoter region. Two polymorphisms were identified: one was the same silent SNP at codon 102 in exon 3 detected by Humar *et al.*, *supra*. and the other was an unidentified SNP in a region of the promoter approximately 600 to 1000 bp upstream of the transcription start site. Spirio *et al.* did not disclose the nucleotide change or position for the promoter SNP.

The cytochrome P-450 3A4 (CYP3A4) enzyme, expressed in the liver and intestine, is responsible for the oxidative metabolism of a wide variety of xenobiotics, including an estimated 60% of all clinically used drugs. Expression of CYP3A4 is induced by a wide variety of compounds, including many drugs, and this induction is the basis for many common drug interactions. A human nuclear receptor that is activated by known inducers of CYP3A4 and binds to xenobiotic response elements in the CYP3A4 promoter has recently been identified. This nuclear receptor has been classified as NR1I2 (nuclear receptor subfamily 1, group I, member 2) and is commonly known as pregnane X receptor, SXR (steroid and xenobiotic receptor) or PAR. Human NR1I2 cDNAs have been cloned and sequenced by several groups. Lehman *et al.*, J. Clin. Invest., 1998, vol. 102, pages 1016-1023, isolated a series of NR1I2 clones from a human liver cDNA library. Bertilsson *et al.*, Proc. Natl. Acad. Sci. U S A, 1998, vol. 95, pages 12208-12213, identified two cDNAs for the human NR1I2 gene by searching for homologous sequences in an expression sequence tag (EST) database for orphan nuclear receptors. The two cDNAs differed in their 5' end. Blumberg *et al.*, Genes Dev., 1998, vol. 12, pages 3195-3205, used the homologous *Xenopus* BXR gene as a probe to identify the gene for NR1I2 from a human liver cDNA library. The sequence reported by Blumberg *et al.* differed from that reported by both Lehman *et al.* and Bertilsson *et al.* by a nucleotide substitution resulting in a proline rather than a serine at codon 187 (CCT>TCT). In addition, the cDNA isolated by Blumberg *et al.* showed the deletion of an adenine in codon 214, which would result in a frameshift from amino acid 215 to 233, at which point the insertion of a guanine resumed the amino acid sequence identity. Dotzlaw *et al.*, Clin. Cancer Res., 1999, vol. 5, pages 2103-2107, found that both NR1I2 and a variant NR1I2 mRNA were expressed in normal and neoplastic human breast tissue samples. The authors performed PCR analysis covering a region from nucleotide 678 to 1119 (using the numbering of Lehman *et al.*). The normal NR1I2 mRNA is 442 nucleotides long and identical in sequence to that reported by Lehman *et al.*, while the variant NR1I2 differed by the deletion of 111 nucleotides corresponding to nucleotides 823 to 933 (amino acids 174 to 210) in the ligand binding domain.

The glutathione S-transferases (GSTs) comprise a superfamily of enzymes that catalyze Phase II conjugation of glutathione with a variety of xenobiotics and their reactive metabolites. Cytosolic GSTs are dimeric proteins composed of 3 classes of subunits, classified according to protein sequence similarity and antibody crossreactivity. In addition to multiple cytosolic GST families, there exists a microsomal membrane-bound transferase referred to as microsomal glutathione S-transferase 1 (GST12) and has limited sequence homology with cytosolic GSTs.

DeJong *et al.*, J. Biol. Chem., 1988, vol. 263, pages 430-436, screened a human liver cDNA library with a rat microsomal GST cDNA and identified cDNA sequences encoding GST12. Northern blot analysis showed that GST12 in the liver was expressed as a 0.95-kb mRNA. DeJong *et al.*, Genomics, 1990, vol. 6, pages 379-382, used their cDNA to characterize the GST12 gene by genomic blotting and assigned the gene to chromosome 12 by study of a panel of mouse-human somatic cell hybrid DNAs. Kelner *et al.*, Genomics, 1996, vol. 36, pages 100-103, reported the genomic structure of the human GST12 gene. The authors reported that GST12 spanned 12.8 kb and consisted of four exons and three introns, with the entire coding sequence residing on exons 2, 3, and 4. Two nucleotide differences were detected by Kelner *et al.*, *ibid.*, in the exons of genomic GST12 compared to the cDNA sequence reported by DeJong *et al.* in J. Biol. Chem., *ibid.* A cytosine in the third position of codon 73 of the cDNA sequence was guanine in the genomic sequence, a silent change, and an adenine to guanine change in the 3' untranslated region of the genomic sequence (exon 4) was also detected. Lee and DeJong, Biochim. Biophys. Acta, 1999, vol. 1446, pages 389-396, concluded that the structure and organization GST12 was more complex than the earlier report of Kelner *et al.*, *supra*. Lee and DeJong determined that the human GST12 gene spanned 18 kb and comprised seven exons which they called Ia, Ib, Ic, Id, II, III, and IV. Exons Id – IV corresponded to the previously reported gene structure and exons Ia through Ic encoded alternative 5'UTR sequences. The authors concluded that exons Ia, Ib, Ic, Id, and III are alternatively spliced to generate at least six different GST12 transcripts, with the predominant transcript containing exon Ib. Kelner *et al.*, J. Biol. Chem., 2000, vol. 275, pages 13000-13006, re-examined the human GST12 gene structure and organization, and corrected their earlier report. The authors identified transcripts containing either one of only two alternative first exons, IB or ID, and concluded that clones containing exons 1A and 1C identified by Lee and DeJong were either artifactual or nonfunctional. The region between IB and ID was unavailable to direct transcription. One common promoter directing transcription of GST12 was found, and RNA splicing appeared to occur by "mutually exclusive exon splicing" such that only one type of exon 1 would be incorporated into each mRNA. The predominant liver transcript contained exon 1B, and the GST12 promoter region just upstream of this exon responded to oxidative stress.

Multidrug resistance (MDR) proteins (MRPs) effect the ATP-dependent transport of drugs from normal cells and tumors. The MRP3 (HUGO name: ABCC3) gene product is known to confer resistance to multiple cancer chemotherapeutic agents by increasing drug efflux. Kool *et al.*, Cancer Res., 1997, vol. 57, pages 3537-3547, searched an EST library and identified MRP3.

5 Kiuchi *et al.*, FEBS Lett., 1998, vol. 433, pages 149-152, cloned and expressed a full-length human MRP3 cDNA from Caco-2 cells. Belinsky *et al.*, J. Natl. Cancer Inst., 1998, vol. 90, pages 1735-1741, used an EST probe to isolate a 5.2 kb MDR3 cDNA, which they called MOAT-D (multispecific organic anion transporter D) from human liver and monocyte libraries. Uchiyama *et al.*, Biochem. Biophys. Res. Commun., 1998, vol. 252, pages 103-110, isolated a 5.5 kb MRP3

10 cDNA from a human liver library. Fromm *et al.*, Biochim. Biophys. Acta, 1999, vol. 1415, pages 369-374, isolated three different full-length clones for MRP3 from a human liver cDNA library. One clone (that they called MRP3) had an open reading frame showing very close identity to the sequence reported by Kiuchi *et al.*, *ibid.* Fromm *et al.* also identified two splice variants they called MRP3A and MRP3B. The splice variant termed MRP3A contained an additional 149 bp in

15 the coding sequence, leading to a premature stop codon and a predicted polypeptide size of 1238 amino acids. The second splice variant, MRP3B, contained the insert detected in MRP3A plus an additional 55 bp insert, leading to a different premature stop codon and a predicted polypeptide size of 510 amino acids. Using portions of their clones, Fromm *et al.* searched the GenBank database and identified a previously uncharacterized genomic clone, which had been sequenced

20 for the Human Genome Project. The clone was a partial MRP3 gene spanning 33.6 kb and containing more than 20 kb of 5' flanking region and 14 exons. The additional sequences found in the splice variants were contained within the MRP3 genomic sequences, indicating that alternative splicing of MRP3 may occur by incomplete removal of intron sequences. Konig *et al.*, Hepatology, 1999, vol. 29, pages 1156-1163, cloned MRP3 cDNAs from a human liver cDNA

25 library, including one splice variant that lacked 192 bp corresponding to the region comprising amino acids 270 to 333. By means of transport studies with polarized MDCKII canine kidney cells as well as with MRP3 transfection studies, Kool *et al.*, Proc. Natl. Acad. Sci. USA, 1999, vol. 96, pages 6914-6919, showed that MRP3 is an organic ion and multidrug transporter that localizes to basolateral cell membranes. The authors cloned a human liver MRP3 cDNA and used

30 it to generate several stable MRP3-transfected cell lines. In addition, MDCKII canine kidney cells overexpressing ABCC3 mediated transport of the organic anion S-(2,4-dinitrophenyl)-glutathione to the basolateral side of the cell monolayer. The authors suggested that ABCC3 might function as a bile salt transporter on the hepatic and intestinal basolateral membranes. Takada *et al.*, Biochem. Biophys. Res. Commun., 2000, vol. 270, pages 728-732, cloned and characterized the 5'

35 flanking region of MDR3 isolated from a human peripheral blood leukocyte library. The

transcription start site was determined to be 25 to 27 nucleotides upstream of the translation start site.

Certain tumor cells are resistant to multiple lipophilic, structurally related cytotoxic drugs. Two human genes (*mdr1* and *mdr2*) encoding multidrug-resistance export proteins have been  
5 identified. These proteins are transmembrane proteins that transport substances into or out of the intracellular environment in an energy-dependent manner.

The *mdr1* gene, referred to as MDR1, has been localized to chromosome 7 (Fojo *et al.*, Proc. Natl. Acad. Sci. U S A., 1986, vol. 84, pages 265-269). Callen *et al.*, Hum. Genet., 1987, vol. 77, pages 142-144, localized the MDR1 locus to 7q21.1 by *in situ* hybridization. Riordan *et al.*, Nature, 1985, vol. 316, pages 817-819, cloned a cDNA molecule encoding MDR1. Kioka *et al.*, Biochem Biophys Res Commun., 1989, vol. 14, pages 224-231, isolated a full-length MDR1  
10 cDNA from normal human adrenal cells. Chen *et al.*, J Biol Chem., 1990, vol. 265, pages 506-514, characterized the MDR1 genomic sequence indicating that it has 28 exons and encodes a 4.5-kb mRNA.

15 Sequence changes in the MDR1 gene have been identified associated with increased expression. Choi *et al.*, J. Biol. Chem., 1997, vol. 272, pages 5974-5982, identified a sequence mutation that resulted in the substitution of a Gly for a Val at codon 185. The amino acid substitution influences the transport of P-glycoprotein-bound drugs to the outside of a cell. Hoffmeyer *et al.*, Proc. Natl. Acad. Sci. U S A, 2000, vol. 97, pages 3473-3478, identified a  
20 wobble replacement at position 3435 of exon 26 that resulted in a change from C to T and was correlated with the altered expression levels. Stein *et al.*, Eur. J. Cancer, 1994, vol. 30A, pages 1541-1545, identified two polymorphisms that resulted in a change from a T to a C and a G to a T at position 103 and 137, respectively, in the promoter region of the gene. Expression of the MDR1 gene containing the T to C mutation at position 103 was increased in cancer cells upon  
25 treatment with anticancer drugs such as vincristine and doxorubicin. Rund *et al.*, Adv. Exp. Med. Biol., 1999, vol. 457, pages 71-51, identified a polymorphism that resulted in a nucleotide change of a T to a C at position 8 in the 5' untranslated region. Yoshimoto *et al.*, Nucleic Acids Res., 1988, vol. 16, page 11850, identified a polymorphic *HindIII* restriction enzyme site in the MDR1 gene. Decleves *et al.*, Hum. Mutat., 2000, vol. 15, pages 486-487, identified a missense mutation  
30 resulting in a nucleotide change of an A to a G at position 485 of exon 2 resulting in amino acid change of an asparagine to aspartate.

In mammals, UDP-glucuronosyltransferases (UGTs) comprise a gene. These genes produce proteins that are responsible for the detoxification or inactivation of numerous endogenous and xenobiotic compounds, including many carcinogens. UGTs catalyze the transfer  
35 of a glucuronic acid moiety to their substrates, thereby converting them to more water-soluble



forms that can be more readily excreted in bile or urine. Two families of UGTs have been recognized based on protein sequence similarity, UGT1 and UGT2.

Jackson *et al.*, *Biochem. J.*, 1987 vol. 242, pages 581-588, cloned a human liver microsomal UDP-glucuronosyltransferase cDNA that they called HLUG 25. The entire sequence was 2104 nucleotides long, including a poly-A tail and a long open reading frame. Jin *et al.*, *Biochem. Biophys. Res. Commun.*, 1993, vol. 194, pages 496-503, isolated cDNAs encoding for two UDP-glucuronosyltransferases, UGT2B4 and UGT2B10 by screening a liver library with a rat UGT2B1 cDNA. Monaghan *et al.*, *Mamm. Genome*, 1997, vol. 8, pages 692-694, determined the genomic structure of UGT2B4, reporting an identical intron-exon organization identical to that of the rat UGT2B gene family, which contains 6 exons and 5 introns. Beaulieu *et al.*, *Biochem. Biophys. Res. Commun.*, 1998, vol. 248, pages 44-50, isolated a human prostate cDNA referred to as UGT2B11. Levesque *et al.*, *Pharmacogenetics*, 1999, vol. 9, pages 207-216, isolated a human several UGT2B4 cDNA variants from normal prostate or prostate cancer cell cDNA libraries. One variant, called UGT2B4(E<sup>458</sup>) by the authors, had two nucleotide differences that would result in an amino acid change of glutamate to aspartate at codon 458.

The microsomal UGT2B7 enzyme has unique specificity for 3,4-catechol estrogens and estriol, suggesting that it may play an important role in regulating the level and activity of these potent estrogen metabolites. Ritter *et al.*, *J. Biol. Chem.*, 1990, vol. 265, pages 7900-7906, isolated a human cDNA clone encoding a 529 amino acid protein corresponding to UGT2B7 from liver cDNA library. Jin *et al.*, *J. Pharmacol. Exp. Ther.*, 1993, vol. 264, pages 475-479, isolated a variant human liver UGT2B7 cDNA clone that encoded a protein differing in only one amino acid, tyrosine for histidine at codon 268. Coffman *et al.*, *Drug Metab. Dispos.*, 1997, vol. 25, pages 1-4, isolated the variant human liver UGT2B7 cDNA encoding a tyrosine at codon 268. Carrier *et al.*, *Biochem. Biophys. Res. Commun.*, 2000, vol. 272, pages 616-621, determined the structure of the human UGT2B7 gene and characterized 500 nucleotides of the promoter region. Ishii *et al.*, *Mol. Pharmacol.*, 2000, vol. 57, pages 940-947, characterized 900 nucleotides of the human UGT2B7 promoter region.

Coffman *et al.*, *Arch. Biochem. Biophys.*, 1990, vol. 281, pages 170-175, isolated a partial cDNA for UGT2B15, which they referred to as HLUG4 or UGT2B8. Chen *et al.*, *Biochemistry*, 1993, vol. 32, pages 10648-10657, subsequently cloned a human liver cDNA they called UDPGTh-3 that was 96% identical to the cDNA of Coffman *et al.*, *ibid.* A third human liver UGT2B15 cDNA was isolated by Green *et al.*, *Drug Metab. Dispos.*, 1994, vol. 22, pages 799-805, that was identical in nucleotide sequence to the cDNA of Chen *et al.* Green *et al.* reported that the partial clone of Coffman *et al.* was missing the first 21 nucleotides that encoded 7 amino acids of the leader sequence. Levesque *et al.*, *Pharmacogenetics*, 1997, vol. 7, pages 317-325, isolated a prostate UGT2B15 cDNA that varied from the previously reported UGT2B15 cDNAs

of Chen *et al.* and Green *et al.* by 20 nucleotides, none of which were in the 5' untranslated region. Two of the nucleotide changes were in the coding region, although one was silent change. The predicted amino acid sequence differed only at one codon, resulting in the substitution of a tyrosine for an aspartic acid at position 85. Turgeon *et al.*, J. Mol. Biol., 2000, vol. 295, pages 489-504, isolated and characterized the human UGT2B15 gene and 2.5 kb of 5' flanking region. UGT2B15 consisted of 6 exons spanning approximately 25 kb, and exhibited a high degree of nucleotide sequence and structural homology to the human UGT2B17 gene.

#### SUMMARY OF THE INVENTION

The present invention relates to novel polymorphisms located in various human genes and the use of those polymorphisms as predictive sequences for altered metabolism, the occurrence of disease, or as markers for genetic linkage analysis. According to the present invention there are provided cytochrome P450 1A1, cytochrome P450 1A2, cytochrome P450 2E1, adrenergic receptor B1, aryl hydrocarbon receptor, aryl hydrocarbon receptor nuclear translocator, cathepsin S, cyclooxygenase 2, diazepam binding inhibitor, epoxide hydroxylase 2, 5-lipoxygenase activating protein, glutathione-S-transferase 12, histidine-N-methyl transferase, kallikrein 2, nicotinamide-N-methyl transferase, NADPH quinone oxidoreductase 2, sulfotransferase thermolabile, UDP-glucuronosyl transferase 2B4, UDP-glucuronosyl transferase 2B7, UDP-glucuronosyl transferase 2B15, urokinase receptor, multidrug resistance gene 1, lactotransferrin, multidrug resistance associated protein 3, orphan nuclear receptor, acetylcholine muscarinic 1, acetylcholine muscarinic receptor 2, acetylcholine muscarinic receptor 3, acetylcholine muscarinic receptor 4, or acetylcholine muscarinic receptor 5 gene, polymorphic nucleic acid sequences, and methods to use such nucleic acid sequences, in particular for diagnostic purposes to identify individuals having a polymorphic genotype.

Further embodiments of the invention include various methods for identifying polymorphisms. One such method is a method for identifying a polymorphism in a nucleic acid molecule of an individual which includes determining whether a nucleic acid sequence selected from SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 72, SEQ ID NO: 74, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 98, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 150, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 160, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 168, SEQ ID NO: 170, SEQ ID NO: 172, SEQ ID NO: 205, SEQ ID NO: 207, SEQ ID NO: 209, SEQ ID NO:

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907, SEQ ID NO: 909, SEQ ID NO: 911, SEQ ID NO: 913, SEQ ID NO: 915, SEQ ID NO: 917, SEQ ID NO: 982, SEQ ID NO: 984, SEQ ID NO: 986, SEQ ID NO: 988, SEQ ID NO: 990, SEQ ID NO: 992, SEQ ID NO: 994, SEQ ID NO: 996, SEQ ID NO: 998, SEQ ID NO: 1000, SEQ ID NO: 1002, SEQ ID NO: 1004, SEQ ID NO: 1006, SEQ ID NO: 1008, SEQ ID NO: 1010, SEQ ID NO: 1012, SEQ ID NO: 1014, SEQ ID NO: 1016, SEQ ID NO: 1018, SEQ ID NO: 1020, SEQ ID NO: 1022, SEQ ID NO: 1024, SEQ ID NO: 1026, SEQ ID NO: 1028, SEQ ID NO: 1030, SEQ ID NO: 1032, SEQ ID NO: 1034, SEQ ID NO: 1036, SEQ ID NO: 1038, SEQ ID NO: 1040, SEQ ID NO: 1042, SEQ ID NO: 1044, SEQ ID NO: 1046, SEQ ID NO: 1048, SEQ ID NO: 1050, SEQ ID NO: 1052, SEQ ID NO: 1054, SEQ ID NO: 1056, SEQ ID NO: 1058, SEQ ID NO: 1060, SEQ ID NO: 1062, SEQ ID NO: 1064, SEQ ID NO: 1121, SEQ ID NO: 1123, SEQ ID NO: 1125, SEQ ID NO: 1127, SEQ ID NO: 1129, SEQ ID NO: 1131, SEQ ID NO: 1133, SEQ ID NO: 1135, SEQ ID NO: 1137, SEQ ID NO: 1139, SEQ ID NO: 1141, SEQ ID NO: 1143, SEQ ID NO: 1145, SEQ ID NO: 1147, SEQ ID NO: 1149, SEQ ID NO: 1151, SEQ ID NO: 1153, SEQ ID NO: 1155, SEQ ID NO: 1157, SEQ ID NO: 1159, SEQ ID NO: 1161, SEQ ID NO: 1163, SEQ ID NO: 1165, SEQ ID NO: 1167, SEQ ID NO: 1169, SEQ ID NO: 1171, SEQ ID NO: 1173, SEQ ID NO: 1175, SEQ ID NO: 1177, SEQ ID NO: 1179, SEQ ID NO: 1181, SEQ ID NO: 1183, SEQ ID NO: 1185, SEQ ID NO: 1187, SEQ ID NO: 1189, SEQ ID NO: 1191, SEQ ID NO: 1193, SEQ ID NO: 1195, SEQ ID NO: 1197, SEQ ID NO: 1199, SEQ ID NO: 1201, SEQ ID NO: 1262, SEQ ID NO: 1264, SEQ ID NO: 1266, SEQ ID NO: 1268, SEQ ID NO: 1270, SEQ ID NO: 1272, SEQ ID NO: 1274, SEQ ID NO: 1276, SEQ ID NO: 1278, SEQ ID NO: 1280, SEQ ID NO: 1282, SEQ ID NO: 1284, SEQ ID NO: 1286, SEQ ID NO: 1288, SEQ ID NO: 1290, SEQ ID NO: 1292, SEQ ID NO: 1294, SEQ ID NO: 1296, SEQ ID NO: 1298, SEQ ID NO: 1300, SEQ ID NO: 1302, SEQ ID NO: 1304, SEQ ID NO: 1306, SEQ ID NO: 1308, SEQ ID NO: 1310, SEQ ID NO: 1312, SEQ ID NO: 1314, SEQ ID NO: 1316, SEQ ID NO: 1318, SEQ ID NO: 1320, SEQ ID NO: 1322, NO: 1346, SEQ ID NO: 1348, SEQ ID NO: 1350, SEQ ID NO: 1352, SEQ ID NO: 1354, SEQ ID NO: 1356, SEQ ID NO: 1358, SEQ ID NO: 1360, SEQ ID NO: 1362, SEQ ID NO: 1364, SEQ ID NO: 1366, SEQ ID NO: 1368, SEQ ID NO: 1370, SEQ ID NO: 1372, SEQ ID NO: 1374, SEQ ID NO: 1376, SEQ ID NO: 1390, SEQ ID NO: 1392, SEQ ID NO: 1394, SEQ ID NO: 1401, SEQ ID NO: 1418, SEQ ID NO: 1420, SEQ ID NO: 1422, SEQ ID NO: 1424, SEQ ID NO: 1426, SEQ ID NO: 1435, SEQ ID NO: 1437, SEQ ID NO: 1439, and SEQ ID NO: 1446 or a nucleic acid sequence that is fully complementary thereto is present in the nucleic acid molecule. Another method includes a method for evaluating alteration in an individual's drug metabolism, immunological, hematological, pulmonary, cardiovascular or central nervous system function, or risk of developing cancer. These methods include obtaining a nucleic acid molecule sample from said individual.

The methods further include determining whether one of the newly identified polymorphisms in the genes encoding cytochrome P450 1A1 protein, cytochrome P450 1A2 protein, cytochrome P450 2E1 protein, adrenergic receptor B1 protein, aryl hydrocarbon receptor protein, aryl hydrocarbon receptor nuclear translocator protein, cathepsin S, cyclooxygenase 2 protein, diazepam binding inhibitor protein, epoxide hydroxylase 2 protein, 5-lipoxygenase activating protein, glutathione-S-transferase 12 protein, histamine-N-methyl transferase protein, kalleikrin 2 protein, nicotinamide-N-methyl transferase protein, NADPH quinone oxidoreductase 2 protein, sulfotransferase thermolabile protein, UDP-glucuronosyl transferase 2B4 protein, UDP-glucuronosyl transferase 2B7 protein, UDP-glucuronosyl transferase 2B15 protein, urokinase protein, multidrug resistance gene 1 protein, lactoferrin protein, multidrug resistance associated protein 3 protein, orphan nuclear receptor protein, acetylcholine muscarinic 1 protein, acetylcholine muscarinic receptor 2 protein, acetylcholine muscarinic receptor 3 protein, acetylcholine muscarinic receptor 4 protein, or acetylcholine muscarinic receptor 5 protein is present in a human nucleic acid sample.

The methods of the present invention can further include determining whether an individual is homozygous or heterozygous for a given nucleic acid sequence. Such methods can either be a cDNA assay or a genomic DNA assay. Such methods can also include a step of digesting a nucleic acid molecule sequence with a restriction enzyme that distinguishes between a polymorphic nucleic acid sequence and the corresponding wildtype sequence. Further, the methods can include amplifying a selected region of the nucleic acid molecule of the individual.

Additional embodiments of the present invention include kits for conducting the various methods. Such kits can include nucleic acid molecules of the present invention, as well as restriction enzymes useful in the methods.

## 25 DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to compositions that contain certain genetic characteristics and methods that reveal the presence or absence of such characteristics. The present invention includes the identification of different genetic polymorphisms in the cytochrome P450 1A1 (CYP4501A1), cytochrome P450 1A2 (CYP4501A2), cytochrome P450 2E1 (CYP4502E1), adrenergic receptor B1 (ADRB1), aryl hydrocarbon receptor (AHR), aryl hydrocarbon receptor nuclear translocator (ARNT), cathepsin S (CTSS), cyclooxygenase 2 (COX2), diazepam binding inhibitor (DBI), epoxide hydroxylase 2 (EPHX), 5-lipoxygenase activating protein (FLAP), glutathione-S-transferase 12 (GST12), histamine-N-methyl transferase (HNMT), kallikrein 2 (KLK2), nicotinamide-N-methyl transferase (NNMT), NADPH quinone oxidoreductase 2 (NQO2), sulfotransferase thermolabile (STM), UDP-glucuronosyl transferase 2B4 (UGT2B4), UDP-glucuronosyl transferase 2B7 (UGT2B7), UDP-glucuronosyl transferase 2B15 (UGT2B15),

urokinase receptor (uPA), multidrug resistance gene 1 (PGY1 or MDR1), lactotransferrin (LTF), multidrug resistance associated protein 3 (MRP3), orphan nuclear receptor (NR1I2), acetylcholine muscarinic receptor 1 (CHMR1), acetylcholine muscarinic receptor 2 (CHMR2), acetylcholine muscarinic receptor 3 (CHMR3), acetylcholine muscarinic receptor 4 (CHMR4), or acetylcholine muscarinic receptor 5 (CHMR5) gene. The presence or absence of the polymorphism at one or more of these sites has been found to be prognostic or diagnostic for different indications as discussed below. Nucleic acid molecules comprising the polymorphic sequences contained in CYP4501A1, CYP4501A2, AHR, MDR1 and/or MDR3 are used to screen individuals for altered drug metabolism or susceptibility to cancer. Nucleic acid molecules comprising the polymorphic sequences contained in CYP4502E1, ARNT, EPHX, GST12, NNMT, NQO2, NR1I2, STM, UGT2B4, UGT2B7 and/or UGT2B15 are used to screen individuals for altered drug metabolism. Nucleic acid molecules comprising the polymorphic sequences contained in ADRB1 or CHMR2 are used to screen individuals for altered cardiovascular function. Nucleic acid molecules comprising the polymorphic sequences contained in CTSS are used to screen individuals for altered pulmonary function. Nucleic acid molecules comprising the polymorphic sequences contained in COX2 are used to screen individuals for altered susceptibility to colorectal tumors. Nucleic acid molecules comprising the polymorphic sequences contained in DBI or CHMR1 are used to screen individuals for altered central nervous system function. Nucleic acid molecules comprising the polymorphic sequences contained in FLAP and HNMT are used to screen individuals for altered pulmonary, immunological or hematological function. Nucleic acid molecules comprising the polymorphic sequences contained in KLK2 are used to screen individuals for altered serine protease activity in the prostate. Nucleic acid molecules comprising the polymorphic sequences contained in urokinase are used to screen individuals for altered coagulation and as a marker for metastatic activity of human tumors. Nucleic acid molecules comprising the polymorphic sequences contained in LTF are used to screen individuals for altered immunological or hematological function. Nucleic acid molecules comprising the polymorphic sequences contained in CHMR3, CHMR4, CHMR5 are used to screen individuals for altered central and peripheral nervous system function.

It is to be understood that the inventions disclosed herein are not limited to the particular methodology, protocols, cell lines, animal species or genera, constructs and reagents described, and as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

For the purposes of the present invention, the term "a" or "an" entity refers to one or more of that entity; for example, "a protein" or "a nucleic acid molecule" refers to one or more of those compounds or at least one compound. As such, the terms "a" (or "an"), "one or more" and "at

least one” can be used interchangeably herein. It is also to be noted that the terms “comprising”, “including”, and “having” can be used interchangeably. Furthermore, a compound “selected from the group consisting of” refers to one or more of the compounds in the list that follows, including mixtures (i.e., combinations) of two or more of the compounds.

5       According to the present invention, reference to an “isolated nucleic acid molecule” refers to a nucleic acid molecule which is the size of, or smaller than, a gene. Thus, an isolated nucleic acid molecule does not encompass isolated genomic DNA or an isolated chromosome. The term isolated nucleic acid molecule does not connote any specific minimum length. It should also be appreciated that reference to an isolated nucleic acid molecule does not necessarily reflect the  
10       extent of purity of the nucleic acid molecule. An isolated nucleic acid molecule of the present invention can be obtained from a natural source, such as a tissue sample, or it can be produced using molecular biology techniques, such as by polymerase chain reaction (PCR) amplification, or it can be produced by chemical synthesis.

      “Allele” has the meaning which is commonly known in the art, that is, a genomic variant  
15       of a referent gene, including variants, which, when translated result in functional or dysfunctional (including non-existent) gene products. The first identified allelic form is arbitrarily designated as the reference form and other allelic forms are designated as alternative or variant alleles. The allelic form occurring most frequently in a selected population is sometimes referred to as the wildtype form.

20       “Contiguously appurtenant to” means any bases flanking the referent position, including the instances of all bases selected 5’ to the referent position and no bases selected 3’ to the referent position; all bases selected 3’ to the referent position and no bases selected 5’ to the referent position; and some bases selected 5’ and some bases selected 3’ to the referent position. The term is intended to mean that the selected bases necessarily must be in the same sequential  
25       order as described in the referent sequence, with the exception of the variant base at the referent position.

      “For the purpose of determining genotype” means that one of the purposes is to determine genotype, not necessarily that the end goal or use of the information is to determine genotype. For instance, “for the purpose of determining genotype” includes the use of the information to  
30       determine genotype for the ultimate goal of determining the probability of negative or positive drug interactions.

      “Gene” has the meaning that is commonly-known in the art, that is, a nucleic acid sequence that includes the translated sequences that code for a protein (“exons”) and the untranslated intervening sequences (“introns”), and any regulatory elements ordinarily necessary  
35       to translate the protein.

"Genotype" has the meaning that is commonly known in the art, that is, a physical description of a nucleic acid sequence.

"Hybridization" has the meaning that is commonly known in the art, that is, the formation of a duplex structure by two single-stranded nucleic acids due to complementary base pairing.

5 Hybridization can occur between exactly complementary nucleic acid strands or between nucleic acid strands that contain some regions of mismatch.

"Polymorphism" means a polymorphism wherein the group exists by virtue of a difference in identity of one or more nucleotides at given sequence locations. The location of nucleotide identity differences is usually preceded by and followed by highly conserved sequences (e.g.,  
10 sequences that vary in less than 1/100 or 1/1000 members of the populations). However, more than one single nucleotide polymorphism can exist between or among the group members. A "transition" is the replacement of one purine by another purine or one pyrimidine by another pyrimidine. A "transversion" is the replacement of a purine by a pyrimidine or vice versa. Single nucleotide polymorphisms can also arise from a deletion of a nucleotide or an insertion of a  
15 nucleotide relative to a given sequence location.

"Stringent hybridization" means that which is commonly known in the art, that is, at a salt concentration of no more than 1M and a temperature of at least 25 degrees Celsius. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM Sodium Phosphate, 5 mM EDTA, pH 7.4) and a temperature of 55 to 60 degrees Celsius are suitable.

20 In the present invention, alleles are expressed by symbols in accordance with definitions given by IUPAC-IUB and common names or common usage in the art.

The wildtype CYP4501A1 gene encodes an enzyme called cytochrome P450 1A1 protein. The wildtype CYP4501A2 gene encodes an enzyme called cytochrome P450 1A2 protein. The wildtype CYP4502E1 gene encodes an enzyme called cytochrome P450 2E1 protein. The  
25 wildtype ADRB1 gene encodes a protein called adrenergic receptor B1 protein. The wildtype AHR gene encodes a protein called aryl hydrocarbon receptor protein. The wildtype ARNT gene encodes a protein called aryl hydrocarbon receptor nuclear translocator protein. The wildtype CTSS gene encodes a protein called cathepsin S protein. The wildtype COX2 gene encodes an enzyme called cyclooxygenase 2 protein. The wildtype DBI gene encodes a protein called  
30 diazepam binding inhibitor protein. The wildtype EPHX2 gene encodes an enzyme called epoxide hydroxylase 2 protein. The wildtype FLAP gene encodes an enzyme called 5-lipoxygenase activating protein. The wildtype GST12 gene encodes an enzyme called glutathione-S-transferase 12 protein. The wildtype HNMT gene encodes an enzyme called histamine-N-methyl transferase protein. The wildtype KLK2 gene encodes a protein called kallikrein 2 protein. The wildtype  
35 NNMT gene encodes an enzyme called nicotinamide-N-methyl transferase protein. The wildtype NQO2 gene encodes an enzyme called NADPH quinone oxidoreductase 2 protein. The wildtype



STM gene encodes a protein called sulfotransferase thermolabile protein. The wildtype UGT2B4 gene encodes an enzyme called UDP-glucuronosyl transferase 2B4 protein. The wildtype UGT2B7 gene encodes an enzyme called UDP-glucuronosyl transferase 2B7 protein. The wildtype UGT2B15 gene encodes an enzyme called UDP-glucuronosyl transferase 2B15 protein.

- 5 The wildtype uPA gene encodes an enzyme called urokinase protein. The wildtype MDR1 gene encodes a protein called multidrug resistance gene 1 protein. The wildtype LTF gene encodes a protein called lactotransferrin protein. The wildtype MRP3 gene encodes a protein called multidrug resistance associated protein 3. The wildtype NR1I2 gene encodes a protein called orphan nuclear receptor protein. The wildtype CHMR1 gene encodes a protein called
- 10 acetylcholine muscarinic receptor 1 protein. The wildtype CHMR2 gene encodes a protein called acetylcholine muscarinic receptor 2 protein. The wildtype CHMR3 gene encodes a protein called acetylcholine muscarinic receptor 3 protein. The wildtype CHMR4 gene encodes a protein called acetylcholine muscarinic receptor 4 protein. The wildtype CHMR5 gene encodes a protein called acetylcholine muscarinic receptor 5 protein.

- 15 One embodiment of the present invention is an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 72, SEQ ID NO: 74, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID NO: 80, SEQ
- 20 ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 98, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 150, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 160, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 168, SEQ ID NO: 170, SEQ ID NO: 172, SEQ ID NO:
- 25 205, SEQ ID NO: 207, SEQ ID NO: 209, SEQ ID NO: 211, SEQ ID NO: 213, SEQ ID NO: 215, SEQ ID NO: 217, SEQ ID NO: 219, SEQ ID NO: 249, SEQ ID NO: 251, SEQ ID NO: 253, SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 297, SEQ ID NO: 299, SEQ ID NO: 301, SEQ ID NO: 303, SEQ ID NO: 305, SEQ ID NO: 307, SEQ ID NO: 309, SEQ ID NO: 311, SEQ ID NO: 313, SEQ ID NO: 315, SEQ ID NO: 317,
- 30 SEQ ID NO: 319, SEQ ID NO: 321, SEQ ID NO: 323, SEQ ID NO: 325, SEQ ID NO: 327, SEQ ID NO: 329, SEQ ID NO: 331, SEQ ID NO: 340, SEQ ID NO: 342, SEQ ID NO: 344, SEQ ID NO: 346, SEQ ID NO: 348, SEQ ID NO: 350, SEQ ID NO: 352, SEQ ID NO: 354, SEQ ID NO: 393, SEQ ID NO: 395, SEQ ID NO: 397, SEQ ID NO: 399, SEQ ID NO: 401, SEQ ID NO: 403, SEQ ID NO: 405, SEQ ID NO: 407, SEQ ID NO: 409, SEQ ID NO: 411, SEQ ID NO: 413, SEQ
- 35 ID NO: 415, SEQ ID NO: 417, SEQ ID NO: 419, SEQ ID NO: 421, SEQ ID NO: 423, SEQ ID NO: 425, SEQ ID NO: 427, SEQ ID NO: 429, SEQ ID NO: 431, SEQ ID NO: 433, SEQ ID NO:

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NO: 1394, SEQ ID NO: 1401, SEQ ID NO: 1418, SEQ ID NO: 1420, SEQ ID NO: 1422, SEQ ID  
NO: 1424, SEQ ID NO: 1426, SEQ ID NO: 1435, SEQ ID NO: 1437, SEQ ID NO: 1439, and SEQ  
ID NO: 1446 and a nucleic acid sequence that is fully complementary to such a nucleic acid  
20 sequence. In accordance with the present invention, an isolated nucleic acid molecule is a nucleic  
acid molecule that has been removed from its natural milieu (i.e., that has been subject to human  
manipulation) and can include DNA, RNA, or derivatives of either DNA or RNA. An isolated  
nucleic acid molecule of the present invention can be isolated from its natural source or can be  
produced using recombinant DNA technology (e.g., polymerase chain reaction amplification,  
25 cloning) or chemical synthesis. The nucleic acid molecules of the present invention are isolated  
and obtained in substantial purity, generally as other than an intact chromosome. Usually, the  
nucleic acid molecule will be obtained substantially free of other nucleic acid sequences that do  
not include a nucleic acid molecule sequence of the present invention (e.g., a CYP1A1 sequence,  
or a CYP1A2 sequences, and so on) or fragment thereof, generally being at least about 50%,  
30 usually at least about 90% pure. Although the phrase "nucleic acid molecule" primarily refers to  
the physical nucleic acid molecule and the phrase "nucleic acid sequence" primarily refers to the  
sequence of nucleotides on the nucleic acid molecule, the two phrases can be used  
interchangeably.

The nucleic acid sequence of the CYP4501A1 genomic gene is generally known in the art  
35 and accessible in public databases as cited above. For example, GenBank Accession No. X04300  
identifies the human CYP4501A1 gene, GenBank Accession Nos. M31664, U02993, M31665,

M31666 and M31667 identify the human CYP4501A2 gene, GenBank Accession No. D10014 identifies the human CYP4502E1 gene, GenBank Accession No. J03019 identifies the human ADRB1 gene, GenBank Accession Nos. D31708, U27657, U28060, D38044, L19872, U28064 and U28065 identify the human AHR gene, GenBank Accession Nos. U07369, U07370, U07371, 5 U07372 and U07374 identify the human CTSS gene, GenBank Accession No. U04636 identifies the human COX2 gene, GenBank Accession No. X94563 identifies the human DBI gene, GenBank Accession Nos. X97024, X97025, X97026, X97027, X97028, X97029, X97030, X97031, X97032, X97033, X97034, X97035, X97036, X97037 and X97038 identify the human EPHX2 gene, GenBank Accession Nos. M60470, M63259, M63260 and M63261 identify the 10 human FLAP gene, GenBank Accession Nos. U46495, U46497, U46498 and M63261 identify the human GST12 gene, GenBank Accession Nos. U44106, U44107, U44108, U44109, U44110 and U44111 identify the human HNMT gene, GenBank Accession No. M18157 identifies the human KLK2 gene, GenBank Accession Nos. U20970 and U20971 identifies the human NNMT gene, GenBank Accession No. U20499 identifies the human STM gene, GenBank Accession No. 15 X02419 identifies the human uPA gene, GenBank Accession Nos. AC002457, M57450, AC002457 and AC005068 identify the human MDR1 gene, GenBank Accession No. AC002457 identifies the human LTF gene, GenBank Accession No. AC004590 identifies the human MRP3 gene, GenBank Accession No. Y00508/M35128 identifies the human CHMR1 gene, GenBank Accession No. M16404 identifies the human CHMR2 gene, GenBank Accession No. U29589 20 identifies the human CHMR3 gene, GenBank Accession No. M16405 identifies the human CHMR4 gene, and GenBank Accession No. M80333 identifies the human CHMR5 gene. Each genomic sequence is useful as a reference for the genomic location of a polymorphism within a particular gene or for specific coding region sequences. As used herein, the term "CYP4501A1 gene" is intended to refer to both the wildtype and polymorphic sequences, unless specifically 25 denoted otherwise. Nucleic acids of particular interest comprise the provided polymorphic sequences. It is within the skill of one in the art to identify the location of a polymorphic sequence of the present invention using wildtype genomic or cDNA sequences known in the art. A skilled artisan can use a polymorphic sequence, its corresponding wildtype sequence and the sequence contiguously appurtenant to the referenced polymorphism provided in Tables 3, 6, 9, 12, 30 15, 18, 21, 24, 26, 28, 31, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81, 84 and 87 with a known genomic sequence or cDNA sequence to determine the position of the polymorphism. It is within the scope of the invention that a polymorphism includes detection at the designated genomic sequence nucleotide position or its corresponding cDNA position if the polymorphism is located within the coding region of a sequence.

35 In accordance with the present invention, the polymorphisms in the CYP4501A1 gene occur at nucleotides -1602, -1579, -1315, -1060, -1034, -1019, -976, -946 and -468 of the promoter

region of the CYP4501A1 gene. For the purposes of identification in this application, the positions of the polymorphisms of the CYP4501A1 promotor region are referenced as the nucleotide positions preceding the transcription start site as identified in Kawajiri *et al*, Eur. J. Biochem, 159, p. 219-225 (1986).

5        Regarding positions -1602, -1579, -1315, -1060, -1034, -1019, -976, -946 and -468 of the promoter region, the polymorphism is typically one or more base substitutions such as T to A, A to G, G to A, C to G, G to A, T to G, G to T, G to A and G to A, respectively. These polymorphisms are silent.

10        The polymorphisms of the CYP4501A2 gene sequence occur at nucleotide -2216, -1570, -906, -810 of the promoter region of the CYP4501A2 genomic sequence or nucleotide 821 of intron 1, nucleotide 62 of exon 2, nucleotide 525 of intron 2, nucleotide 63 of exon 3, or nucleotide 43 of intron 4, or nucleotide 201 of intron 4, or nucleotide 81 of intron 6, or nucleotide 292 of exon 7. For the purposes of identification in this application, the positions of the polymorphisms of the CYP4501A1 promotor region are referenced as the nucleotide positions  
15        delineated in Ikeya *et al*, Mol. Endo. 3(9), p.1399-1408 (1989). The wildtype sequences are shown in SEQ ID NOs: 85-88. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding cytochrome P450 1A2 protein.

20        In the case of positions -2216, -906, -810 of the promoter region the polymorphism is typically one or more base substitutions such as G to A, A to G and T to C, respectively. In the case of positions 821, 525, 43, 201, 81 (in introns 1, 2, 4, 4 or 6, respectively) the polymorphism is typically one or more base substitutions such as T to G, G to A, A to G, G to C and T to C, respectively. In the case of positions 62 in exon 2, 63 in exon 3, and 292 in exon 7, the polymorphism is typically one or more base substitutions such as C to G, C to A and T to C,  
25        respectively. At position -1570 of the promoter region, the polymorphism is typically the deletion of a T.

30        The polymorphisms of the CYP4502E1 gene sequence occur at nucleotide -969, -894, -376, -326, -316, -299 or -297 of the promoter region. The wildtype sequence is shown in SEQ ID NO: 111. For the purposes of identification in this application, the positions of the polymorphisms of the CYP4502E1 promotor region are referenced as the number of nucleotide positions 5' to the transcription start site identified by Umeno *et al*, Biochemistry 27, p.9006-13 (1988). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding cytochrome P450 2E1 protein.

In the case of positions -969, -894, -376, -326, -316, -299 and -297 of the promoter region the polymorphism is typically one or more base substitutions such as A to G, A to G, T to C, C to T, A to G, G to C and T to A, respectively.

Polymorphisms of the ADRB1 gene occur at nucleotide positions 145, 315, 1165 or 1347  
5 of the ADRB1 cDNA, or nucleotide 8 of the 3' UTR. The wildtype cDNA sequence is shown in SEQ ID NO: 132. For the purposes of identification in this application, the positions of the polymorphisms of the ADRB1 cDNA are referenced as the number of nucleotide positions after the initial A in the start methionine in the coding sequence as isolated by Frielle et al., PNAS, 84, p.7920-24 (1987).

10 In the case of positions 145, 315, 1165 and 1347 of the cDNA, the polymorphism is typically one or more base substitutions such as A to G, G to T, G to C, C to G and C to A, respectively. In the case of position 8 of the 3' UTR, the polymorphism is typically one or more base substitutions such as C to A.

The polymorphisms of the AHR gene occur at nucleotide 119, 152, 157 and 240 of the 5'  
15 UTR, or nucleotide 132 of exon 2, or nucleotide 33 of intron 3, or nucleotide 771 of exon 7, or nucleotide 33 of intron 7, or nucleotide 1192 of exon 10, or nucleotide 1411, 1664 and 1738 of exon 10. By identifying the location of a polymorphism in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the aryl hydrocarbon receptor protein.

20 In the case of positions 119, 152, 157 and 240 of the 5' UTR, the polymorphism is typically one or more base substitutions such as C to T, G to A, G to A or C to G, respectively. In the case of position 132 of exon 2, the polymorphism is typically one or more base substitutions such as T to C. In the case of position 33 of intron 3, the polymorphism is typically the deletion of the bases AG. In the case of positions 132, 771, 1192, 1411, 1664 and 1738, the polymorphism is  
25 typically one or more base substitutions such as T to C, A to T, C to A, C to T, G to A, and G to A, respectively.

The polymorphisms of the ARNT gene sequence occur at nucleotide 97 of intron 3, or nucleotide 123 of intron 4, or nucleotide 667 of exon 5, or nucleotide 18 of intron 8, or nucleotide 103 of intron 10, or nucleotide -74 of intron 16, or nucleotide -60 of intron 17, or nucleotide 6 of  
30 the 3' UTR. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the aryl hydrocarbon receptor protein.

In the case of positions 97, 123, 667, 18, 103, -74 and 6, the polymorphism is typically one or more base substitutions such as T to C, G to A, G to C, T to G, G to A, ACTCTC to  
35 TCACCTA and T to C, respectively. In the case of position -60, the polymorphism is typically the deletion of a base such as an A.

The polymorphisms of the CTSS gene sequence occur at nucleotide -521, -359, -246 of the promoter region, or nucleotide 41 or 44 of the 5' UTR, or nucleotide 88 of exon 2, or nucleotide 405 of exon 4, or nucleotide -47 of intron 4. The wildtype sequence of CTSS is shown in SEQ ID Nos: 264-269. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the cathepsin S protein.

In the case of positions -521, -359, 41, 44, 88, 405 and -47 of the promoter region the polymorphism is typically one or more base substitutions such as A to G and C to T, T to C, A to G, T to C, C to T and C to T, respectively. In the case of positions -246 of the promoter, the polymorphism is typically a deletion of the bases TCCC.

The polymorphisms of the COX2 gene sequence occur at nucleotide -763, -653 or -605 of the promoter region, or nucleotide 306 of exon 3, or nucleotide 437 of exon 4, or nucleotide 38 of intron 6, or nucleotide -25 of intron 6, or nucleotides 732 or 900 of exon 7, or nucleotide 111 of intron 7, or nucleotide 1209 of exon 8, or nucleotide 72 of intron 9, or nucleotide 1532 or 1759 of exon 10, or nucleotide 277, 427, 629 or 678 of the 3' UTR. The wildtype sequence of COX2 is shown in SEQ ID NO: 332 as identified by Appleby *et al*, Structure of the human cyclooxygenase-2 gene, Biochem. J., 302, p. 723-27 (1994). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the cyclooxygenase 2 protein.

The polymorphisms at positions -763, -605, 38, 111, 72, 306, 437, 732, 900, 1209, 1532, 1759, are typically one or more base substitutions such as G to C, T to C, G to A, T to C, C to T, C to G, C to T, T to C, T to C, T to C, T to C, T to C, and G to A, respectively. In the case of positions 427, 629 and 678 of the 3' UTR, the polymorphism is typically one or more base substitutions such as T to C, G to C and A to G, respectively. In the case of position -653 of the promoter, the polymorphism is typically an insertion of bases such as TAG. In the case of position -25 of intron 6, the polymorphism is typically a deletion of bases such as TTTA. In the case of position 277 of the 3' UTR, the polymorphism is typically a deletion of bases such as TTATA.

The polymorphisms of the DBI gene sequence occur at nucleotide -144 of the promoter region, or nucleotides -148, -106, -77 or -53 of intron 1A, or nucleotides 29, 55 or 92 of intron 2. The wildtype sequence of DBI is shown in SEQ ID NO: 355 as described by Swinnen *et al*, A human gene encoding diazepam-binding inhibitor/acyl-CoA-binding protein: transcription and hormonal regulation in the androgen-sensitive human prostatic adenocarcinoma cell line LNCaP, J. DNA Cell Biol., 15 (3), 197-208 (1996). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding

nucleotide in the coding region of a cDNA sequence encoding the diazepam-binding inhibitor protein.

In the case of positions -144 of the promoter region the polymorphism is typically one or more base substitutions such as G to A. In the case of positions -148, -106, -77, -53, 29, 55 and 92  
5 of intron 1 the polymorphism is typically one or more base substitutions such as A to G, G to A, C to T, G to A, C to A, C to T and G to C, respectively.

The polymorphisms of the EPHX2 gene sequence occur at nucleotides 68 or -81 of intron 1, or nucleotide 164 of exon 2, or nucleotide 307 of exon 3, or nucleotides 31, 49 or 136 of intron 3, or nucleotides 461 or 489 of exon 4, or nucleotides 5 or 25 of intron 4, or nucleotide 591 of  
10 exon 5, or nucleotides 21 or -19 of intron 5, or nucleotide 687 of exon 6, or nucleotide 25 of intron 6, or nucleotides 69 or -32 of intron 7, or nucleotide 860 of exon 8, or nucleotides 8, -100 or -97 of intron 8, or nucleotide -5 of intron 9, or nucleotide -44 of intron 12, or nucleotides 1209, 1236 or 1237 of exon 13, or nucleotides 15, -65 or -60 of intron 13, or nucleotide 1275 of exon 14, or nucleotide 148 of intron 15, or nucleotides 52, 114 or -124 of intron 16, or nucleotides 35 or -  
15 99 of intron 17, or nucleotide 1593 of exon 19, or nucleotides 35 or 93 of the 3' UTR. The wildtype sequence of EPHX2 is shown in SEQ ID NOs: 472-486 as described by Beetham *et al*, cDNA Cloning and Expression of a Soluble Epoxide Hydrolase from Human Liver, Arch. Biochem. Biophys., 305 (1), p. 197-201 (1993). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the  
20 corresponding nucleotide in the coding region of a cDNA sequence encoding the human soluble epoxide hydrolase protein.

In the case of positions 68 and -81 of intron 1, the polymorphism is typically one or more base substitutions such as A to G and A to G, respectively. In the case of position 164 of exon 2, the polymorphism is typically a base substitution such as A to G. In the case of position 307 of  
25 exon 3, the polymorphism is typically a base substitution such as C to T. In the case of positions 31, 49 and 136 of intron 3, the polymorphism is typically one or more base substitutions such as C to T, C to T and C to A, respectively. In the case of positions 461 and 489 of exon 4, the polymorphism is typically one or more base substitutions such as G to A and T to A, respectively. In the case of positions 5 and 25 of intron 4, the polymorphism is typically one or more base  
30 substitutions such as G to A and G to C, respectively. In the case of position 591 of exon 5, the polymorphism is typically a base substitution such as A to C. In the case of positions 21 and -19 of intron 5, the polymorphism is typically one or more base substitutions such as G to A and A to G, respectively. In the case of position 687 of exon 6, the polymorphism is typically a base substitution such as G to A. In the case of position 25 of intron 6, the polymorphism is typically a  
35 base substitution such as G to A. In the case of positions 69 and -32 of intron 7, the polymorphism is typically one or more base substitutions such as G to A and A to T, respectively. In the case of



position 860 of exon 8, the polymorphism is typically a base substitution such as G to A. In the case of position 8 of intron 8, the polymorphism is typically a base substitution such as T to C. In the case of position -5 of intron 9, the polymorphism is typically a base substitution such as C to T. In the case of position -44 of intron 12, the polymorphism is typically a base substitution such as C to T. In the case of positions 1236 and 1237 of exon 13, the polymorphism is typically one or more base substitutions such as C to T and G to A, respectively. In the case of positions 15, -65 and -60 of intron 13, the polymorphism is typically one or more base substitutions such as T to C, G to T, and G to A, respectively. In the case of position 1275 of exon 14, the polymorphism is typically a base substitution such as G to A. In the case of position 148 of intron 15, the polymorphism is typically a base substitution such as C to T. In the case of positions 52, 114 and -124 of intron 16, the polymorphism is typically one or more base substitutions such as G to A, G to A and G to A, respectively. In the case of positions 68 and -81 of intron 1, the polymorphism is typically one or more base substitutions such as A to G and A to G, respectively. At positions 35 and 93 of the 3' UTR, the polymorphism is typically one or more base substitutions such as A to G and T to C, respectively.

The polymorphisms of the 5-lipoxygenase activating protein (FLAP) gene occur at nucleotides -500, -263, -240 of the promoter region of the FLAP genomic sequence or nucleotide 18 of intron 1, or nucleotide 12, 87, or 95 of intron 2, or nucleotide 64 of intron 3. The wildtype sequence is listed in SEQ ID NOs: 525-527 and described by Kennedy *et al*, Gene characterization and promoter analysis of the human 5-Lipoxygenase-activating protein (FLAP), J. Biol. Chem. 266, 8511-8516 (1991). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the 5-Lipoxygenase-activating protein.

In the case of positions -263 and -240 of the promoter region, the polymorphism is typically one or more base substitutions such as G to A, or A to C, respectively. In the case of position 18 of intron 1, the polymorphism is typically one or more base substitutions such as C to A. In the case of positions 12, 87, and 95 of intron 2, the polymorphism is typically one or more base substitutions such as C to A, G to A, or T to C, respectively. At position 64 of intron 3, the polymorphism is typically one or more base substitutions such as G to T. In the case of position -500 of the promoter region, the polymorphism is typically a deletion of bases such as TG. In the case of position +51 of the 5' UTR, the polymorphism is typically one or more base substitutions such as C to T. In the case of position +219 of the 3' UTR, the polymorphism is typically one or more base substitutions such as A to G.

The polymorphisms of the glutathione-S-transferase 12 (GST12) gene occur at nucleotide -26 of intron 1, or nucleotide -84 of intron 2, nucleotide -19 of intron 3, or nucleotides 19 or 57 of the 3' UTR. The wildtype sequence is listed in SEQ ID NOs: 545-547 and described in Kelner *et*

*al*, Structural Organization of the Human Microsomal Glutathione S-Transferase Gene (GST12), Genomics, 36, 100-03 (1996). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the GST12 protein.

5       At position -26 of intron 1, the polymorphism is typically one or more base substitutions such as T to C. At position -84 of intron 2, the polymorphism is typically one or more base substitutions such as C to G. At position -19 of intron 3, the polymorphism is typically one or more base substitutions such as T to C. At positions +19 and +57 of the 3'UTR, the polymorphism is typically one or more base substitutions such as G to A, or T to G, respectively.

10       The polymorphisms of the histamine-N-methyl transferase (HNMT) gene occur at nucleotides -490, -458, -320, -211, -159, and -125 of the promoter region of the HNMT gene or nucleotide +108 of the 5' UTR, or nucleotide -128 of intron 1, or nucleotide +137 of intron 3, or nucleotide +48 of intron 4, or nucleotide 314 of exon 4, or nucleotides +60 or +218 of the 3' UTR. The wildtype sequence is listed in SEQ ID NOs:592-597 and described by Aksoy *et al*, Human  
15 histamine N-methyltransferase gene: structural characterization and chromosomal location, Biochem. Biophys. Res. Commun., 219 (2), 548-554 (1996). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the histamine N-methyltransferase protein.

20       In the case of positions -490, -320, -211, -159, -125 of the promoter region the polymorphism is typically one or more base substitutions such as G to C, A to G, T to C, C to T, or T to C, respectively. In the case of position -128 of intron 1, the polymorphism is typically one or more base substitutions such as G to A. In the case of position +137 of intron 3, the polymorphism is typically one or more base substitutions such as C to A. In the case of position  
25 314 of exon 4, the polymorphism is typically one or more base substitutions such as C to T. In the case of position +48 of intron 4, the polymorphism is typically the deletion of the two bases AA. In the case of position +108 of the 5' UTR, the polymorphism is typically one or more base substitutions such as G to A. In the case of position -458 of the promoter region, the polymorphism is typically the deletion of the base A. In the case of positions +60 and +218 of the  
30 3' UTR, the polymorphisms are typically one or more base substitutions such as G to A or T to A, respectively.

      The polymorphisms of the kalleikrin 2 (KLK2) gene occur at nucleotides -214 of the promoter region of the KLK2 gene or nucleotide 62, 115, or -4 of intron 1, or nucleotide 372 of exon 3, or nucleotide 55 or -18 of intron 3, or nucleotide +100 of intron 4, or nucleotide 748 of  
35 exon 5. The wildtype sequence is listed in SEQ ID NO: 634 and described by Schedlich *et al*, Primary Structure of a Human Glandular Kallikrein Gene, DNA 6 (5), 429-37 (1987). By

identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the KLK2 protein.

At position -214 of the promoter region, the polymorphism is typically one or more base substitutions such as G to A. In the case of positions +62, +115, or -4, of intron 1, the polymorphism is typically one or more base substitutions such as C to G, A to G, or G to A, respectively. At positions +55 or -18 of intron 3, the polymorphism is typically one or more base substitutions such as A to G or T to A, respectively. At position 372 of exon 3, the polymorphism is typically one or more base substitutions such as C to T. In the case of position +100 of intron 4, the polymorphism is typically one or more of base substitutions such as C to A. At position 748 of exon 5, the polymorphism is typically one or more base substitutions such as C to T.

The polymorphisms of the nicotinamide-N-methyl transferase (NNMT) gene occur at nucleotides -292 and -228 of the promoter region of the NNMT gene or nucleotide +44 of intron 1, or nucleotide 86 of the 5' UTR, or nucleotide +71 of the 3' UTR. The wildtype sequence is listed in SEQ ID NOs: 655 and 656 and described in Aksoy *et al*, Human Nicotinamide N-methyltransferase Gene: Molecular Cloning, Structural Characterization and Chromosomal Localization, Genomics 29 (3), 555-61 (1995). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the NNMT protein.

In the case of positions -292, or -228 of the promoter region the polymorphism is typically one or more base substitutions such as A to G or A to T, respectively. At position +44 of intron 1 the polymorphism is typically one or more base substitutions such as T to C. At position +86 of the 5' UTR, the polymorphism is typically one or more base substitutions such as C to T. At position +71 of the 3' UTR, the polymorphism is typically one or more base substitutions such as A to G.

The polymorphisms of the NADPH quinone oxidoreductase 2 (NQO2) gene occur at nucleotide -19 of the promoter region of the NQO2 gene or nucleotide 12, 17, -95, or -15 of intron 1, or nucleotide +14 of intron 2, or nucleotide 93, 47, or 139 of exon 3, or nucleotide 36, 59, or -50 of intron 3, or nucleotide 330 or 405 of exon 5, or nucleotide +21 or -107 of intron 5, or nucleotide 438 of exon 6, or nucleotide 84 or 86 of intron 6, or nucleotide +38 of the 3' UTR, or nucleotide +171 of the 5' UTR. The wildtype sequence is listed in SEQ ID NOs: 721-727 and described by Jaiswal *et al*, Biochem. 29, 1899-1906 (1990). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the NQO2 protein.

In the case of positions -19 of the promoter region the polymorphism is typically one or more base substitutions such as A to G. In the case of positions +12, +17, -95, and -15 of intron

1, the polymorphism is typically one or more base substitutions such as C to T, G to A, C to T, or T to C, respectively. At position +14 of intron 2, the polymorphism is typically one or more base substitutions such as A to G. At positions 93, 47, and 139 of exon 3, the polymorphism is typically one or more base substitutions such as C to T, A to G, or T to C, respectively. At positions +36 and +59 of intron 3, the polymorphism is typically one or more base substitutions such as T to C or A to G, respectively. At positions 330 and 405 of exon 5, the polymorphism is typically one or more base substitutions such as G to A or C to T, respectively. At positions +21 and -107 of intron 5, the polymorphism is typically one or more base substitutions such as T to A or A to G, respectively. At position 438 of exon 6, the polymorphism is typically one or more base substitutions such as C to T. At position +84 of intron 6, the polymorphism is typically one or more base substitutions such as A to G. At position +86 of intron 6, the polymorphism is typically one or more base substitutions such as A to G or an insertion of the bases GC or GCAC. At position -50 of intron 3, the polymorphism is typically a deletion of the base G. At position +171 of the 5' UTR, the polymorphism is typically one or more base substitutions such as C to A. At position +38 of the 3'UTR, the polymorphism is typically one or more base substitutions such as G to C.

The polymorphisms of the sulfotransferase thermolabile (STM) gene occur at nucleotide -70 or -64 of intron 1, or nucleotide 105 of exon 4, or nucleotide +367 of the 3' UTR. The wildtype sequence is listed in SEQ ID NO: 745 and described by Aksoy *et al*, Human Thermolabile Phenol Sulfotransferase Gene (STM): Molecular Cloning and Complete Structural Characterization, Biochem. Biophys. Res. Comm., 208, 786-795 (1995). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the STM protein.

In the case of positions -70, and -64 of intron 1, the polymorphism is typically one or more base substitutions such as G to C or C to T, respectively. In the case of position 105 of exon 4, the polymorphism is typically one or more base substitutions such as A to G. At position +367 of the 3' UTR, the polymorphism is typically the deletion of the bases AATT.

The polymorphisms of the UDP-glucuronosyl transferase 2B4 (UGT2B4) gene occur at nucleotides -1818, -1746, -1373, -1217, -1125, -1053, -946, -827, -747, -507, -180, and -125 of the promoter region. The wildtype sequence is listed in SEQ ID NO:789. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the protein.

At positions -1818, -1746, -1373, -1217, -1125, -1053, -946, -827, -747, -507, -180, and -125 of the promoter region, the polymorphism is typically one or more base substitutions such as

G to A, C to T, G to A, A to C, C to T, T to C, A to G, A to T, C to G, C to T, A to T, or G to T, respectively.

The polymorphisms of the UDP-glucuronosyl transferase 2B7 (UGT2B7) gene occur at nucleotide -1099, -886, -721, -520, -313, -147, -124, -111, -18 of the promoter region. The wildtype sequence is listed in SEQ ID NO:826. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the UGT2B7 protein.

In the case of positions -1099, -886, -721, -520, -313, -147, -124, -111, -18 of the promoter region, the polymorphism is typically one or more base substitutions such as T to C, G to A, C to T, G to A, A to G, T to C, G to A, T to C, or C to T, respectively.

The polymorphisms of the UDP-glucuronosyl transferase 2B15 (UGT2B15) gene occur at nucleotides -1399, -1387, -1129, -932, -852, -808, -503, -498, -496, -487, -432, -383, -368, and -207 of the promoter region. The wildtype sequence is listed in SEQ ID NO:867. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the UGT2B15 protein.

In the case of positions -1399, -1387, -1129, -932, -852, -808, -503, -498, -496, -487, -432, -383, -368, -207 of the promoter region the polymorphism is typically one or more base substitutions such as G to A, C to A, C to T, A to C, C to G, G to T, T to C, A to G, A to T, C to T, T to C, G to A, C to T, or G to A, respectively.

The polymorphisms of the urokinase (uPA) gene occur at nucleotide +28 of intron 2, or nucleotide +49 of intron 3, or nucleotide 422 of exon 6, or nucleotide -7 of intron 7, or nucleotide 691 or 822 of exon 8, or nucleotide +66 or -125 intron 9, or nucleotide 22 of the 5'UTR or nucleotide 141, 753, or 844 of the 3'UTR. The wildtype sequence is listed in SEQ ID NO: 918 and described by Riccio *et al*, The Human Urokinase-Plasminogen Activator Gene and its Promoter, Nucleic Acids Res., 13 (8), 2759-2771 (1985). By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the uPA protein.

In the case of positions +28 of intron 1, +49 of intron 3, -7 of intron 7, and +66, and -125 of intron 9, the polymorphism is typically one or more base substitutions such as C to A, G to A, T to C, T to C, or A to G, respectively. In the case of positions 422 of exon 6, 691 of exon 8, and 822 of exon 8, the polymorphism is typically one or more base substitutions such as C to T, A to C, or C to T, respectively. At position +22 of the 5' UTR, the polymorphism is typically a C to A transition. At positions +141 and +753 of the 3' UTR, the polymorphism is typically a T to C or a

C to T transition, respectively. At position +844 of the 3' UTR, the polymorphism is typically the deletion of the base G.

The polymorphisms of the multidrug resistance gene 1 (MDR1) gene occur at nucleotides -479, -299, -1653, -1350, -1210, of the promoter region of the MDR1 gene or  
 5 nucleotide 61 of exon 2, or nucleotide +36 of intron 3, or nucleotide -25 of intron 4, or nucleotide +66 of intron 5, or nucleotide +139 of intron 6, or nucleotide 781 of exon 8, or nucleotide -106 of intron 8, or nucleotide -41 of intron 10, or nucleotide 1236 of exon 12, or nucleotide +44 of intron 12, or nucleotide +24 or +81 of intron 13, or nucleotide +38 of intron 14, or nucleotide +38 of intron 15, or nucleotide +73 of intron 16, or nucleotide -76 of intron 16, or nucleotide -88 of  
 10 intron 18, or nucleotide -35 of intron 18, or nucleotide +129 of intron 19, or nucleotide 2650 of exon 21, or nucleotide 2677 of exon 21, or nucleotide -72 of intron 24, or nucleotide -182 of intron 27, or nucleotide -168 of intron 27, or nucleotide -152 of intron 27, or nucleotide -135 of intron 27, or nucleotide -98 of intron 27, or nucleotide -87 of intron 27, or nucleotide -86 of intron 27. The wildtype sequence is listed in SEQ ID NOs: 1065-1067. By identifying the  
 15 location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the MDR1 protein.

In the case of positions -479, -299, -1653, -1350, -1210 of the promoter region, the polymorphism is typically one or more base substitutions such as T to C, T to C, G to A, G to A,  
 20 or T to C, respectively. At positions +36 of intron 3, -25 of intron 4, +66 of intron 5, +139 of intron 6, -106 of intron 8, -41 of intron 10, +44 of intron 12, +24 of intron 13, +81 of intron 13, +38 of intron 14, +38 of intron 15, +73 of intron 16, -76 of intron 16, -88 of intron 18, -35 of intron 18, +129 of intron 19, -72 of intron 24, -182 of intron 27, -168 of intron 27, -152 of intron 27, -135 of intron 27, -98 of intron 27, -87 of intron 27, and -86 of intron 27, the polymorphism is  
 25 typically one or more base substitutions such as C to T, G to T, T to G, T to C, A to G, T to G, C to T, T to C, C to T, G to A, G to A, A to G, T to A, G to A, G to C, G to A, C to G, G to T, T to C, A to G, T to C, C to T, A to G, and T to C, respectively. In the case of positions 61 of exon 2, 781 of exon 8, 1236 of exon 12, 2650 or 2677 of exon 21, the polymorphism is typically one or more base substitutions such as A to G, A to G, T to C, C to T, and T to G, respectively. At  
 30 position +140 of the 5' UTR, the polymorphism is typically one or more base substitutions such as A to G. At positions +21, +89, +146, +193, and +252 of the 3'UTR the polymorphism is typically one or more base substitutions such as T to C, A to T, G to A, A to G, or A to C, respectively. At positions +79 and +164 of the 3'UTR, the polymorphism is the deletion of the bases TT or insertion of the bases GAGAGACA, respectively.

35 The polymorphisms of the lactoferrin (LTF) gene occur at nucleotides -470, -420, and -398, of the promoter region of the LTF gene or nucleotides 64, 85, or 140 of exon 2, or

nucleotides +46, +81, or -14 of intron 2, or nucleotides +57 or +105 of intron 3, or nucleotide 578 of exon 5, or nucleotides +51 or +80 of intron 5, or nucleotide 661 of exon 6, or nucleotide +37 of intron 7, or nucleotides +49 or +72 of intron 8, or nucleotides 1092, 1110, or 1200 of exon 9, +92, +104, -46, or -125 of intron 9, or nucleotide 1248 of exon 10, or nucleotide +124, +155, or -76 of intron 11, or nucleotide 1623 of exon 13, or nucleotides +34, -6, or -26 of intron 13, or nucleotides +46 or -23 of intron 14, or nucleotides 1737 or 1894 of exon 15, or nucleotide -48 of intron 15, or nucleotides +223, -111, or -107 of intron 16. The wildtype sequence is listed in SEQ ID NOs:1202-1215. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the LTF protein.

In the case of positions -470, -420, -398 of the promoter region the polymorphism is typically one or more base substitutions such as G to A, C to T, and T to A, respectively. In the case of positions +46, +81, of intron 2, +57, +105 of intron 3, +51, +80 of intron 5, +37 of intron 7, +49, +72 of intron 8, +92, +104, -46, -125 of intron 9, +155, -76 of intron 11, +34, -6, -26 of intron 13, +46, -23 of intron 14, -48 of intron 15, +223, -111, -107 of intron 16, the polymorphism is typically one or more base substitutions such as G to T, C to T, G to C, T to C, C to G, G to C, A to T, C to T, C to T, G to C, C to T, G to A, C to T, C to G, C to T, C to A, T to A, T to C, C to T, T to C, T to C, C to T, G to A, and G to A, respectively. In the case of positions 85 or 140 of exon 2, 578 of exon 5, 661 of exon 6, 1092, 1110, or 1200 of exon 9, 1248 of exon 10, 1623 of exon 13, 1737 or 1894 of exon 15, the polymorphism is typically one or more base substitutions such as G to A, A to G, C to T, C to T, C to T, C to T, C to T, A to G, T to C, G to C, and C to T, respectively. At positions 64 of exon 2, -14 of intron 2, and +124 of intron 11, the polymorphism is typically the deletion of the bases AGG, the insertion of the bases GA, or the deletion of the bases TAATTTTAAGGGTGCAA, respectively.

The polymorphisms of the multidrug resistance associated protein 3 (MRP3) gene sequence occur at nucleotide +82 or -53 of intron 3, or nucleotide +73 or -22 of intron 5, or nucleotide -27 or -18 of intron 7, or nucleotide +16 of intron 8, or nucleotide 1820 of exon 14, or nucleotide +110, +208 or -79 of intron 14, or nucleotide +34 or +97 of intron 17, or nucleotide 2293 of exon 18, or nucleotide -63, -28, +95 or -123 of intron 18, or nucleotide 2712 of exon 20, or nucleotide +29 or +53 of intron 20, or nucleotide 3039 of exon 22, or nucleotide +71 of intron 22, or nucleotide -103 of intron 23, or nucleotide -66 of intron 24, or nucleotide +61 of intron 25, or nucleotide 3942 of exon 27, or nucleotide 4042 of exon 28, or nucleotide 4350 of exon 30, or nucleotide +97 of intron 30, or nucleotide 4509 of exon 31. The wildtype sequence is listed in SEQ ID NO:1322. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the MRP3 protein.

In the case of positions +82 and -53 of intron 3, +73 and -22 of intron 5, -27 and -18 of intron 7, +16 intron 8, +110, +208 and -79 of intron 14, +34 and +97 of intron 17, -63, -28, +95 and -123 of intron 18, +29 and +53 of intron 20, +71 of intron 22, -103 of intron 23, -66 of intron 24, +61 of intron 25, +97 of intron 30, the polymorphism is typically one or more base substitutions such as G to A, G to A, C to A, G to A, C to T, C to T, G to A, C to G, T to C, C to T, G to C, G to A, C to T, G to A, C to T, C to T, C to T, G to A, C to T, G to A, C to T, G to A, respectively. In the case of positions 1820 of exon 14, 2293 exon 18, 2712 of exon 20, 3039 of exon 22, 3942 of exon 27, 4042 of exon 28, 4350 of exon 30, 4509 of exon 31, the polymorphism is typically one or more base substitutions such as G to A, G to C, G to A, C to T, C to T, C to T, C to T, or A to G, respectively.

The polymorphisms of the orphan nuclear receptor (NR1I2) gene sequence occur at nucleotides -76 of intron 1, or nucleotide 52 of exon 2, or nucleotide +55, +78 or -29 of intron 2, or nucleotide 696 of exon 5, or nucleotide +52, -91, or -53 intron 5, or nucleotide 834 of exon 6, or nucleotide -17 of intron 6, or nucleotide 1411 of exon 8 or nucleotide 15, 370, 455, or 500 of the 3' UTR. The wildtype sequence is listed in SEQ ID NOs:1377-1382. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the NR1I2 protein.

In the case of positions -76 of intron 1, +55, +78 and -29 of intron 2, +52, -91, and -53 of intron 5, and -17 of intron 6 the polymorphism is typically one or more base substitutions such as G to A, A to G, A to G, C to T, A to G, G to A, C to T, or C to T, respectively. In the case of positions 52 of exon 2, 696 of exon 5, 834 of exon 6, or 1411 of exon 8, the polymorphism is typically one or more base substitutions such as G to A, C to T, G to A, or G to A, respectively. At positions 15, 370, 455, or 500 of the 3'UTR, the polymorphism is typically one or more base substitutions such as G to A, A to G, C to A, and C to A, respectively.

The polymorphisms of the acetylcholine muscarinic receptor 1 (CHMR1) gene sequence occur at nucleotide 267, 1044, or 1353 of exon 1. The wildtype sequence is listed in SEQ ID NO:1395. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the CHMR1 protein.

In the case of positions 267, 1044, or 1353 of exon 1, the polymorphism is typically one or more base substitutions such as C to A, G to A, or C to T, respectively.

The polymorphism of the CHMR2 gene sequence occurs at nucleotide +295 of the 3' UTR. The wildtype sequence is listed in SEQ ID NO:1402. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the CHMR2 protein.



At position +295 of the 3' UTR of the CHMR2 gene, the polymorphism is typically one or more base substitutions such as T to A.

The polymorphisms of the acetylcholine muscarinic receptor 3 (CHMR3) gene occur at nucleotide 168 of exon 1, or nucleotide 144, 418, 700, or 1094 of the 3' UTR. The wildtype sequence is listed in SEQ ID NO:1426. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the CHMR3 protein.

In the case of position 168 of exon 1, the polymorphism is typically one or more base substitutions such as C to T. At positions 144, 418, 700, or 1094 of the 3' UTR the polymorphism is typically one or more base substitutions such as T to C, A to G, C to T, and G to A, respectively.

The polymorphisms of the acetylcholine muscarinic receptor 4 (CHMR4) gene occur at nucleotide -634 of intron 1, or nucleotide 1248 or 1338 of exon 1. The wildtype sequence is listed in SEQ ID NO:1440. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the CHMR4 protein.

In the case of positions -634 of intron 1 the polymorphism is typically one or more base substitutions such as G to T. In the case of positions 1248 or 1338 of exon 1, the polymorphism is typically one or more base substitutions such as C to T.

The polymorphism of the acetylcholine muscarinic receptor 5 (CHMR5) gene occurs at nucleotide 1245 of exon 1. The wildtype sequence is listed in SEQ ID NO:1446. By identifying the location of these polymorphisms in the genomic sequence, it is within the skill of one in the art to determine the corresponding nucleotide in the coding region of a cDNA sequence encoding the CHMR5 protein.

At position 1245 of exon 1, the polymorphism is typically one or more base substitutions such as G to A.

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4501A1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 36 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a G for a C at position 621 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;

- (c) a nucleic acid molecule which comprises an A for a G at position 647 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a G for a T at position 662 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a G at position 705 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises an A for a G at position 735 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a G at position 1213 of SEQ ID NO:31 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:31 contiguously appurtenant to said position; and
- (h) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4501A2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 988 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises the deletion of a T at position 1634 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 2298 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for a T at position 2394 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a G for a T at position 4079 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;

- (f) a nucleic acid molecule which comprises a G for a C at position 4153 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a G at position 5456 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a C at position 5615 of SEQ ID NO:85 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a G for an A at position 133 of SEQ ID NO:86 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:86 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a C for a G at position 291 of SEQ ID NO:86 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:86 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a C for a T at position 168 of SEQ ID NO:87 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:87 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a C for a T at position 763 of SEQ ID NO:88 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:88 contiguously appurtenant to said position; and
- (m) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4502E1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for an A at position 432 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a G for an A at position 507 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a C for a T at position 1025 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;

- (d) a nucleic acid molecule which comprises a T for a C at position 1075 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- 5 (e) a nucleic acid molecule which comprises a G for an A at position 1085 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for a G at position 1102 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- 10 (g) a nucleic acid molecule which comprises an A for a T at position 1104 of SEQ ID NO:111 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:111 contiguously appurtenant to said position; and
- (h) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g).

15 Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human ADRB1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for an A at position 231 of SEQ ID NO:132 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- 20 (b) a nucleic acid molecule which comprises a T for a C at position 401 of SEQ ID NO:132 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a C for a G at position 1251 of SEQ ID NO:132 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- 25 (d) a nucleic acid molecule which comprises a G for a C at position 1433 of SEQ ID NO:132 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises an A for a C at position 1528 of SEQ ID NO:132 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:132 contiguously appurtenant to said position; and
- 30 (f) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e).

Another embodiment of the present invention is an isolated nucleic acid molecule that  
35 comprises at least one base variation from that of a known human AHR sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a T for a C at position 2126 of SEQ ID NO:173 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- 5 (b) a nucleic acid molecule which comprises an A for a G at position 2159 of SEQ ID NO:173 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- 10 (c) a nucleic acid molecule which comprises an A for a G at position 2164 of SEQ ID NO:173 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a G for a C at position 2247 of SEQ ID NO:173 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- 15 (e) a nucleic acid molecule which comprises a C for a T at position 247 of SEQ ID NO:174 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:174 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises the deletion of the bases AG at positions 346 and 347 of SEQ ID NO:175 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:175 contiguously appurtenant to said position;
- 20 (g) a nucleic acid molecule which comprises a T for an A at position 594 of SEQ ID NO:594 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:594 contiguously appurtenant to said position;
- 25 (h) a nucleic acid molecule which comprises a T for a G at position 764 of SEQ ID NO:176 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:176 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises an A for a C at position 202 of SEQ ID NO:177 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
- 30 (j) a nucleic acid molecule which comprises a T for a C at position 421 of SEQ ID NO:177 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises an A for a G at position 671 of SEQ ID NO:177 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
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- (l) a nucleic acid molecule which comprises an A for a G at position 718 of SEQ ID NO:177 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:177 contiguously appurtenant to said position; and
- (m) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l).

5        Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human ARNT sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a T at position 212 of SEQ ID NO:220 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:220 contiguously appurtenant to said position;
- 10        (b) a nucleic acid molecule which comprises an A for a G at position 471 of SEQ ID NO:221 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:221 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a C for a G at position 160 of SEQ ID NO:222 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:222 contiguously appurtenant to said position;
- 15        (d) a nucleic acid molecule which comprises a G for a T at position 142 of SEQ ID NO:225 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:225 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises an A for a G at position 342 of SEQ ID NO:227 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:227 contiguously appurtenant to said position;
- 20        (f) a nucleic acid molecule which comprises the substitution of the bases TCACCTA for the bases ACTCTC at positions 30-35 of SEQ ID NO:232 and at least 20 other bases, alternatively at least 30 other bases of SEQ ID NO:232 contiguously appurtenant to said position;
- 25        (g) a nucleic acid molecule which comprises the deletion of an A at position 62 of SEQ ID NO:233 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:233 contiguously appurtenant to said position;
- 30        (h) a nucleic acid molecule which comprises a C for a T at position 330 of SEQ ID NO:234 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:234 contiguously appurtenant to said position; and
- (i) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CTSS sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- 5 (a) a nucleic acid molecule that comprises a G for an A at position 338 of SEQ ID NO:264 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a T for a C at position 518 of SEQ ID NO:264 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
- 10 (c) a nucleic acid molecule which comprises the deletion of the bases TCCC at positions 610-614 of SEQ ID NO:264 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for a T at position 899 of SEQ ID NO:264 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
- 15 (e) a nucleic acid molecule which comprises a G for an A at position 902 of SEQ ID NO:264 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
- 20 (f) a nucleic acid molecule which comprises a C for a T at position 97 of SEQ ID NO:265 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:265 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises a T for a C at position 178 of SEQ ID NO:267 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:267 contiguously appurtenant to said position;
- 25 (h) a nucleic acid molecule which comprises a T for a C at position 106 of SEQ ID NO:268 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:268 contiguously appurtenant to said position; and
- (i) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h).

30 Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human COX2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for a C at position 69 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
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- (b) a nucleic acid molecule which comprises the insertion of the bases TAG at position 180 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 5 (c) a nucleic acid molecule which comprises a C for a T at position 227 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a G for a C at position 2191 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
10 at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 2975 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises an A for a G at position 4461 of SEQ ID  
15 NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises the deletion of the bases TTTA at positions 4518-4521 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other  
20 bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a C for a T at position 4551 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 25 (i) a nucleic acid molecule which comprises a C for a T at position 4719 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a C for a T at position 4900 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
30 at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a C for a T at position 5310 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 35 (l) a nucleic acid molecule which comprises a T for a C at position 6079 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;



- (m) a nucleic acid molecule which comprises a C for a T at position 6620 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 5 (n) a nucleic acid molecule which comprises an A for a G at position 6847 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 10 (o) a nucleic acid molecule which comprises the deletion of the bases TTATA at positions 7180-7184 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (p) a nucleic acid molecule which comprises a C for a T at position 7330 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 15 (q) a nucleic acid molecule which comprises a C for a G at position 7532 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- (r) a nucleic acid molecule which comprises a G for an A at position 7581 of SEQ ID NO:332 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:332 contiguously appurtenant to said position; and
- 20 (s) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (r).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human DBI sequence, wherein said

25 nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 1020 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- 30 (b) a nucleic acid molecule which comprises a G for an A at position 1610 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises an A for a G at position 1652 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
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- (d) a nucleic acid molecule which comprises a T for a C at position 1681 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- 5 (e) a nucleic acid molecule which comprises an A for a G at position 1705 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- 10 (f) a nucleic acid molecule which comprises an A for a C at position 2532 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises a T for a C at position 2558 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
- 15 (h) a nucleic acid molecule which comprises a C for a G at position 2595 of SEQ ID NO:355 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:355 contiguously appurtenant to said position; and
- (i) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human EPHX sequence, wherein said

20 nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for an A at position 179 of SEQ ID NO:472 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:472 contiguously appurtenant to said position;
- 25 (b) a nucleic acid molecule which comprises a G for an A at position 232 of SEQ ID NO:473 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:473 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 375 of SEQ ID NO:473 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:473 contiguously appurtenant to said position;
- 30 (d) a nucleic acid molecule which comprises a T for a C at position 232 of SEQ ID NO:474 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 302 of SEQ ID NO:474 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or
- 35 at least 50 other bases of SEQ ID NO:474 contiguously appurtenant to said position;

- (f) a nucleic acid molecule which comprises a T for a C at position 320 of SEQ ID NO:474 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- 5 (g) a nucleic acid molecule which comprises an A for a C at position 407 of SEQ ID NO:474 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a C at position 239 of SEQ ID NO:475 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- 10 (i) a nucleic acid molecule which comprises an A for a T at position 267 of SEQ ID NO:475 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises an A for a G at position 320 of SEQ ID NO:475 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- 15 (k) a nucleic acid molecule which comprises a C for a G at position 340 of SEQ ID NO:475 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a C for an A at position 235 of SEQ ID NO:476 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:476 contiguously appurtenant to said position;
- 20 (m) a nucleic acid molecule which comprises an A for a G at position 325 of SEQ ID NO:476 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:476 contiguously appurtenant to said position;
- (n) a nucleic acid molecule which comprises a G for an A at position 204 of SEQ ID NO:477 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- 25 (o) a nucleic acid molecule which comprises an A for a G at position 249 of SEQ ID NO:477 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- 30 (p) a nucleic acid molecule which comprises an A for a G at position 322 of SEQ ID NO:477 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- (q) a nucleic acid molecule which comprises an A for a G at position 283 of SEQ ID NO:478 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
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- (r) a nucleic acid molecule which comprises a T for an A at position 689 of SEQ ID NO:478 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- 5 (s) a nucleic acid molecule which comprises an A for a G at position 749 of SEQ ID NO:478 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- (t) a nucleic acid molecule which comprises a C for a T at position 807 of SEQ ID NO:478 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- 10 (u) a nucleic acid molecule which comprises the deletion of the bases TTT at positions 100-102 of SEQ ID NO:479 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:479 contiguously appurtenant to said position;
- (v) a nucleic acid molecule which comprises the deletion of the bases GTT at positions 103-15 105 of SEQ ID NO:479 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:479 contiguously appurtenant to said position;
- (w) a nucleic acid molecule which comprises a T for a C at position 212 of SEQ ID NO:480 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:480 contiguously appurtenant to said position;
- 20 (x) a nucleic acid molecule which comprises a T for a C at position 189 of SEQ ID NO:483 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- (y) a nucleic acid molecule which comprises the insertion of the bases TCG at position 271 of SEQ ID NO:483 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- 25 (z) a nucleic acid molecule which comprises a T for a C at position 298 of SEQ ID NO:483 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- 30 (aa) a nucleic acid molecule which comprises an A for a G at position 299 of SEQ ID NO:483 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- (bb) a nucleic acid molecule which comprises a C for a T at position 319 of SEQ ID NO:483 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other
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- bases or at least 50 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- (cc) a nucleic acid molecule which comprises a T for a G at position 75 of SEQ ID NO:484 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- (dd) a nucleic acid molecule which comprises an A for a G at position 80 of SEQ ID NO:484 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- (ee) a nucleic acid molecule which comprises an A for a G at position 215 of SEQ ID NO:484 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- (ff) a nucleic acid molecule which comprises a T for a C at position 377 of SEQ ID NO:485 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- (gg) a nucleic acid molecule which comprises an A for a G at position 1167 of SEQ ID NO:485 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- (hh) a nucleic acid molecule which comprises an A for a G at position 1229 of SEQ ID NO:485 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- (ii) a nucleic acid molecule which comprises an A for a G at position 47 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- (jj) a nucleic acid molecule which comprises a T for a C at position 286 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- (kk) a nucleic acid molecule which comprises an A for a C at position 509 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;

- (ll) a nucleic acid molecule which comprises a C for an A at position 869 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- 5 (mm) a nucleic acid molecule which comprises a G for an A at position 979 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- 10 (nn) a nucleic acid molecule which comprises a C for a T at position 1037 of SEQ ID NO:486 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- (oo) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (nn).
- 15 Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human FLAP sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- (a) a nucleic acid molecule that comprises the deletion of the bases TG at positions 200-201 of SEQ ID NO:525 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- 20 (b) a nucleic acid molecule which comprises an A for a G at position 438 of SEQ ID NO:525 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- 25 (c) a nucleic acid molecule which comprises a C for an A at position 461 of SEQ ID NO:525 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a T for a C at position 751 of SEQ ID NO:525 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- 30 (e) a nucleic acid molecule which comprises an A for a C at position 862 of SEQ ID NO:525 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises an A for a G at position 438 of SEQ ID NO:526 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:526 contiguously appurtenant to said position;
- 35

- (g) a nucleic acid molecule which comprises a C for a T at position 446 of SEQ ID NO:526 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:526 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a T for a G at position 301 of SEQ ID NO:527 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:527 contiguously appurtenant to said position; and
- (i) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human GST12 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a T at position 1146 of SEQ ID NO:545 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:545 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a G for a C at position 241 of SEQ ID NO:546 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:546 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a C for a T at position 101 of SEQ ID NO:547 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:547 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises an A for a G at position 385 of SEQ ID NO:547 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:547 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a G for a T at position 423 of SEQ ID NO:547 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:547 contiguously appurtenant to said position; and
- (f) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human HNMT sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a G at position 723 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises the deletion of the base A at position 755 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;

- (c) a nucleic acid molecule which comprises a G for an A at position 893 of SEQ ID NO:893 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:893 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for a T at position 1002 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 1054 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for a T at position 1088 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a G at position 1320 of SEQ ID NO:592 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a G at position 97 of SEQ ID NO:593 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:593 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises an A for a C at position 509 of SEQ ID NO:594 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:594 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a T for a C at position 271 of SEQ ID NO:595 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:595 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises the deletion of the bases AA at positions 434-435 of SEQ ID NO:595 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:595 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises an A for a G at position 663 of SEQ ID NO:597 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:597 contiguously appurtenant to said position; and
- (m) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human KLK2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:



- (a) a nucleic acid molecule that comprises an A for a G at position 281 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a G for a C at position 630 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 683 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises an A for a G at position 1771 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 3689 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a G for an A at position 3865 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a T at position 3906 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a C at position 4160 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a T for a C at position 5571 of SEQ ID NO:634 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:634 contiguously appurtenant to said position; and
- (j) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (i).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human NNMT sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for an A at position 330 of SEQ ID NO:655 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:655 contiguously appurtenant to said position;

- (b) a nucleic acid molecule which comprises a T for an A at position 394 of SEQ ID NO:655 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- 5 (c) a nucleic acid molecule which comprises a T for a C at position 707 of SEQ ID NO:655 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for a T at position 928 of SEQ ID NO:655 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- 10 (e) a nucleic acid molecule which comprises a G for an A at position 643 of SEQ ID NO:656 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:656 contiguously appurtenant to said position; and
- (f) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e).

Another embodiment of the present invention is an isolated nucleic acid molecule that  
15 comprises at least one base variation from that of a known human NQO2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a G for an A at position 1318 of SEQ ID NO:721 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
20 at least 50 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a C at position 1507 of SEQ ID NO:721 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a T for a C at position 1536 of SEQ ID NO:721  
25 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises an A for a C at position 1541 of SEQ ID NO:721 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- 30 (e) a nucleic acid molecule which comprises a T for a C at position 218 of SEQ ID NO:722 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:722 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for a T at position 298 of SEQ ID NO:722  
35 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:722 contiguously appurtenant to said position;

- (g) a nucleic acid molecule which comprises a G for an A at position 418 of SEQ ID NO:722 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:722 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a T for a C at position 326 of SEQ ID NO:723  
5 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a G for an A at position 280 of SEQ ID NO:723 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a C for a T at position 372 of SEQ ID NO:723  
10 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a C for a T at position 441 of SEQ ID NO:723 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
15 at least 50 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a G for an A at position 464 of SEQ ID NO:723 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- (m) a nucleic acid molecule which comprises the deletion of the base G at position 80 of SEQ  
20 ID NO:724 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:794 contiguously appurtenant to said position;
- (n) a nucleic acid molecule which comprises an A for a G at position 202 of SEQ ID NO:725 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
25 at least 50 other bases of SEQ ID NO:725 contiguously appurtenant to said position;
- (o) a nucleic acid molecule which comprises a T for a C at position 277 of SEQ ID NO:725 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:725 contiguously appurtenant to said position;
- (p) a nucleic acid molecule which comprises an A for a T at position 310 of SEQ ID NO:725  
30 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:725 contiguously appurtenant to said position;
- (q) a nucleic acid molecule which comprises a G for an A at position 78 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;

- (r) a nucleic acid molecule which comprises a T for a C at position 214 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- (s) a nucleic acid molecule which comprises a G for an A at position 379 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- (t) a nucleic acid molecule which comprises a G for an A at position 381 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- (u) a nucleic acid molecule which comprises the insertion of the bases GC at position 381 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- (v) a nucleic acid molecule which comprises the insertion of the bases GCAC at position 381 of SEQ ID NO:726 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- (w) a nucleic acid molecule which comprises a C for a G at position 322 of SEQ ID NO:727 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:727 contiguously appurtenant to said position; and
- (x) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (w).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human STM sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a G at position 835 of SEQ ID NO:745 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a T for a C at position 841 of SEQ ID NO:745 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 4465 of SEQ ID NO:745 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises the deletion of the bases AATT at positions 7930-7933 of SEQ ID NO:745 and at least 20 other bases, alternatively at least 30 other

bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:745 contiguously appurtenant to said position; and

- (e) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (d).

Another embodiment of the present invention is an isolated nucleic acid molecule that  
5 comprises at least one base variation from that of a known human UGT2B4 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 5227 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- 10 (b) a nucleic acid molecule which comprises a T for a C at position 5229 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises an A for a G at position 5671 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other  
15 bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for an A at position 5827 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- 20 (e) a nucleic acid molecule which comprises a T for a C at position 5919 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for a T at position 5994 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
25 at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises a G for an A at position 6101 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- 30 (h) a nucleic acid molecule which comprises a T for an A at position 6220 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a G for a C at position 6299 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or  
35 at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;

- (j) a nucleic acid molecule which comprises a T for a C at position 6539 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a T for an A at position 6866 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a T for a G at position 6921 of SEQ ID NO:789 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:789 contiguously appurtenant to said position; and
- (m) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human UGT2B7 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a T at position 33 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a G at position 247 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a T for a C at position 412 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises an A for a G at position 613 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a G for an A at position 820 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for a T at position 986 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a G at position 1009 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;

- (h) a nucleic acid molecule which comprises a C for a T at position 1022 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a T for a C at position 1115 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:826 contiguously appurtenant to said position; and
- (j) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (i).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human UGT2B15 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 95 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a C at position 107 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a T for a C at position 365 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a C for an A at position 562 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a G for a C at position 642 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a T for a G at position 686 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises a C for a T at position 991 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a G for an A at position 996 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;

- (i) a nucleic acid molecule which comprises a T for an A at position 998 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- 5 (j) a nucleic acid molecule which comprises a T for a C at position 1007 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a C for a T at position 1062 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- 10 (l) a nucleic acid molecule which comprises an A for a G at position 1111 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- (m) a nucleic acid molecule which comprises a T for a C at position 1126 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
- 15 (n) a nucleic acid molecule which comprises an A for a G at position 1287 of SEQ ID NO:867 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:867 contiguously appurtenant to said position; and
- 20 (o) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (n).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human uPA sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- 25 (a) a nucleic acid molecule that comprises an A for a C at position 1209 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a C at position 1312 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 30 (c) a nucleic acid molecule which comprises an A for a G at position 1775 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;



- (d) a nucleic acid molecule which comprises a T for a C at position 3005 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 5 (e) a nucleic acid molecule which comprises a C for a T at position 3635 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a C for an A at position 3652 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 10 (g) a nucleic acid molecule which comprises a T for a C at position 3783 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a C for a T at position 4662 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 15 (i) a nucleic acid molecule which comprises a G for an A at position 4818 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 20 (j) a nucleic acid molecule which comprises a C for a T at position 6398 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a T for a C at position 7011 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
- 25 (l) a nucleic acid molecule which comprises the deletion of the base G at position 7103 of SEQ ID NO:918 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:918 contiguously appurtenant to said position; and
- 30 (m) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human MDR1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a C for a T at position 614 of SEQ ID NO:1065 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1065 contiguously appurtenant to said position;
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- (b) a nucleic acid molecule which comprises a C for a T at position 794 of SEQ ID NO:1065 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1065 contiguously appurtenant to said position;
- 5 (c) a nucleic acid molecule which comprises an A for a G at position 370 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- 10 (d) a nucleic acid molecule which comprises an A for a G at position 672 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a C for a T at position 812 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- 15 (f) a nucleic acid molecule which comprises a G for an A at position 2723 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- 20 (g) a nucleic acid molecule which comprises a G for an A at position 2783 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a T for a C at position 7177 of SEQ ID NO:1066 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- 25 (i) a nucleic acid molecule which comprises a T for a G at position 24899 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 30 (j) a nucleic acid molecule which comprises a G for a T at position 25052 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 35 (k) a nucleic acid molecule which comprises a C for a T at position 28523 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other

bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;

- 5 (l) a nucleic acid molecule which comprises a G for an A at position 33860 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 10 (m) a nucleic acid molecule which comprises a G for an A at position 41131 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 15 (n) a nucleic acid molecule which comprises a G for a T at position 44550 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 20 (o) a nucleic acid molecule which comprises a C for a T at position 44884 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 25 (p) a nucleic acid molecule which comprises a T for a C at position 45042 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 30 (q) a nucleic acid molecule which comprises a C for a T at position 45342 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- 35 (r) a nucleic acid molecule which comprises a T for a C at position 4539 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- (s) a nucleic acid molecule which comprises an A for a G at position 45859 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- (t) a nucleic acid molecule which comprises an A for a G at position 49344 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other

bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;

(u) a nucleic acid molecule which comprises a G for an A at position 50419 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;

(v) a nucleic acid molecule which comprises an A for a T at position 50818 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;

(w) a nucleic acid molecule which comprises a T for a C at position 48842 of SEQ ID NO:1067 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1067 contiguously appurtenant to said position; and

(x) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (w).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human LTF sequence, wherein said nucleic acid molecule is selected from the group consisting of:

(a) a nucleic acid molecule that comprises an A for a G at position 48 of SEQ ID NO:1202 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;

(b) a nucleic acid molecule which comprises a T for a C at position 98 of SEQ ID NO:1202 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;

(c) a nucleic acid molecule which comprises an A for a T at position 120 of SEQ ID NO:1202 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;

(d) a nucleic acid molecule which comprises the deletion of the bases AGG at positions 21-23 of SEQ ID NO:1203 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;

(e) a nucleic acid molecule which comprises an A for a G at position 45 of SEQ ID NO:1203 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;

(f) a nucleic acid molecule which comprises a G for an A at position 100 of SEQ ID NO:1203 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other

bases or at least 50 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;

- (g) a nucleic acid molecule which comprises a T for a G at position 213 of SEQ ID NO:1203 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a T for a G at position 248 of SEQ ID NO:1203 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises the insertion of the bases GA at position 114 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a C for a G at position 293 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a C for a T at position 341 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a T for a C at position 1151 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (m) a nucleic acid molecule which comprises a G for a C at position 1274 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (n) a nucleic acid molecule which comprises a C for a G at position 1303 of SEQ ID NO:1204 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- (o) a nucleic acid molecule which comprises a T for a C at position 209 of SEQ ID NO:1205 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1205 contiguously appurtenant to said position;
- (p) a nucleic acid molecule which comprises a T for an A at position 367 of SEQ ID NO:1206 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1206 contiguously appurtenant to said position;
- (q) a nucleic acid molecule which comprises a T for a C at position 409 of SEQ ID NO:1207 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1207 contiguously appurtenant to said position;

- (r) a nucleic acid molecule which comprises a T for a C at position 432 of SEQ ID NO:1207 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1207 contiguously appurtenant to said position;
- 5 (s) a nucleic acid molecule which comprises a T for a C at position 108 of SEQ ID NO:1208 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- (t) a nucleic acid molecule which comprises a T for a C at position 126 of SEQ ID NO:1208 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- 10 (u) a nucleic acid molecule which comprises a T for a C at position 216 of SEQ ID NO:1208 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- (v) a nucleic acid molecule which comprises a C for a G at position 320 of SEQ ID NO:1208 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- 15 (w) a nucleic acid molecule which comprises a T for a C at position 332 of SEQ ID NO:1208 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- (x) a nucleic acid molecule which comprises an A for a G at position 120 of SEQ ID NO:1209 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
- 20 (y) a nucleic acid molecule which comprises a T for a C at position 41 of SEQ ID NO:1209 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
- 25 (z) a nucleic acid molecule which comprises a G for an A at position 202 of SEQ ID NO:1209 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
- 30 (aa) a nucleic acid molecule which comprises the deletion of the bases TAATTTTAAGGGTGCAA at positions 359-375 of SEQ ID NO:1210 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1210 contiguously appurtenant to said positions;
- (bb) a nucleic acid molecule which comprises a G for a C at position 388 of SEQ ID NO:1210 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other
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bases or at least 50 other bases of SEQ ID NO:1210 contiguously appurtenant to said position;

- 5 (cc) a nucleic acid molecule which comprises a T for a C at position 44 of SEQ ID NO:1211 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1211 contiguously appurtenant to said position;
- (dd) a nucleic acid molecule which comprises a C for a T at position 285 of SEQ ID NO:1212 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1212 contiguously appurtenant to said position;
- 10 (ee) a nucleic acid molecule which comprises an A for a C at position 351 of SEQ ID NO:1212 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1212 contiguously appurtenant to said position;
- (ff) a nucleic acid molecule which comprises an A for a T at position 222 of SEQ ID NO:1213 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- 15 (gg) a nucleic acid molecule which comprises a C for a T at position 202 of SEQ ID NO:1213 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- 20 (hh) a nucleic acid molecule which comprises a T for a C at position 341 of SEQ ID NO:1213 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- 25 (ii) a nucleic acid molecule which comprises a C for a T at position 98 of SEQ ID NO:1214 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
- (jj) a nucleic acid molecule which comprises a C for a G at position 134 of SEQ ID NO:1214 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
- 30 (kk) a nucleic acid molecule which comprises a T for a C at position 291 of SEQ ID NO:1214 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
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- (il) a nucleic acid molecule which comprises a C for a T at position 63 of SEQ ID NO:1215 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1215 contiguously appurtenant to said position;
- 5 (mm) a nucleic acid molecule which comprises a T for a C at position 523 of SEQ ID NO:1215 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1215 contiguously appurtenant to said position;
- (nn) a nucleic acid molecule which comprises an A for a G at position 61 of SEQ ID  
10 NO:1216 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1216 contiguously appurtenant to said position;
- (oo) a nucleic acid molecule which comprises an A for a G at position 65 of SEQ ID  
15 NO:1216 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1216 contiguously appurtenant to said position; and
- (pp) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (oo).

Another embodiment of the present invention is an isolated nucleic acid molecule that  
20 comprises at least one base variation from that of a known human MRP3 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 23544 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said  
25 position;
- (b) a nucleic acid molecule which comprises an A for a G at position 23627 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- 30 (c) a nucleic acid molecule which comprises an A for a C at position 24912 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises an A for a G at position 25045 of SEQ ID  
35 NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other



- bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 27526 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a T for a C at position 27535 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises an A for a G at position 759 of SEQ ID NO:1323 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a G at position 1883 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a G for a C at position 2043 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a C for a T at position 2141 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises a T for a C at position 2190 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises an A for a G at position 22978 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (m) a nucleic acid molecule which comprises an A for a G at position 3041 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

- (n) a nucleic acid molecule which comprises a C for a G at position 6438 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 5 (o) a nucleic acid molecule which comprises a T for a C at position 6822 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 10 (p) a nucleic acid molecule which comprises an A for a G at position 6857 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (q) a nucleic acid molecule which comprises a T for a C at position 7169 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 15 (r) a nucleic acid molecule which comprises a T for a C at position 8655 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 20 (s) a nucleic acid molecule which comprises an A for a G at position 8890 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (t) a nucleic acid molecule which comprises a T for a C at position 8921 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 25 (u) a nucleic acid molecule which comprises an A for a G at position 8945 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- (v) a nucleic acid molecule which comprises a T for a C at position 9478 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 30 (w) a nucleic acid molecule which comprises a T for a C at position 9577 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;
- 35 (x) a nucleic acid molecule which comprises an A for a G at position 11057 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other

bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(y) a nucleic acid molecule which comprises a T for a C at position 11443 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(z) a nucleic acid molecule which comprises a T for a C at position 11696 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(aa) a nucleic acid molecule which comprises a T for a C at position 17160 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(bb) a nucleic acid molecule which comprises a T for a C at position 17452 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(cc) a nucleic acid molecule which comprises a T for a C at position 21021 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(dd) a nucleic acid molecule which comprises a T for a C at position 21243 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position;

(ee) a nucleic acid molecule which comprises a G for an A at position 24541 of SEQ ID NO:1448 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1448 contiguously appurtenant to said position; and,

(ff) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human NR112 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a G at position 248 of SEQ ID NO:1377 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a G at position 397 of SEQ ID NO:1377 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 597 of SEQ ID NO:1377 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a G for an A at position 620 of SEQ ID NO:1377 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises a T for a C at position 224 of SEQ ID NO:1378 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1378 contiguously appurtenant to said position;
- (f) a nucleic acid molecule which comprises a T for a C at position 467 of SEQ ID NO:1380 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1380 contiguously appurtenant to said position;
- (g) a nucleic acid molecule which comprises a G for an A at position 617 of SEQ ID NO:1380 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1380 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises an A for a G at position 208 of SEQ ID NO:1381 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a T for a C at position 248 of SEQ ID NO:1381 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises an A for a G at position 340 of SEQ ID NO:1381 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;

- (k) a nucleic acid molecule which comprises a T for a C at position 666 of SEQ ID NO:1381 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises an A for a G at position 1082 of SEQ ID NO:1381 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- (m) a nucleic acid molecule which comprises an A for a G at position 402 of SEQ ID NO:1382 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- (n) a nucleic acid molecule which comprises a G for an A at position 757 of SEQ ID NO:1382 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- (o) a nucleic acid molecule which comprises an A for a C at position 832 of SEQ ID NO:1382 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- (p) a nucleic acid molecule which comprises an A for a C at position 887 of SEQ ID NO:1382 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1382 contiguously appurtenant to said position; and
- (q) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (p).
- Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- (a) a nucleic acid molecule that comprises an A for a C at position 717 of SEQ ID NO:1395 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1395 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises an A for a G at position 1494 of SEQ ID NO:1395 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1395 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a T for a C at position 1803 of SEQ ID NO:1395 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1395 contiguously appurtenant to said position; and
- (d) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (c).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises an A for a T at position 1890 of SEQ ID NO:1402 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1402 contiguously appurtenant to said position; and
- (b) a nucleic acid which is fully complementary to a nucleic acid molecule of (a).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR3 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a T for a C at position 369 of SEQ ID NO1427 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- (b) a nucleic acid molecule which comprises a C for a T at position 2118 of SEQ ID NO1427 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- (c) a nucleic acid molecule which comprises a G for an A at position 2392 of SEQ ID NO1427 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- (d) a nucleic acid molecule which comprises a T for a C at position 2674 of SEQ ID NO1427 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- (e) a nucleic acid molecule which comprises an A for a G at position 2601 of SEQ ID NO1427 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO1427 contiguously appurtenant to said position; and
- (f) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR4 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (a) a nucleic acid molecule that comprises a T for a G at position 138 of SEQ ID NO:1440 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1440 contiguously appurtenant to said position;

(b) a nucleic acid molecule which comprises a T for a C at position 2048 of SEQ ID NO:1440 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1440 contiguously appurtenant to said position;

(c) a nucleic acid molecule which comprises a T for a C at position 2138 of SEQ ID NO:1440  
5 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1440 contiguously appurtenant to said position; and  
(d) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (c).

Another embodiment of the present invention is an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR5 sequence, wherein said  
10 nucleic acid molecule is selected from the group consisting of:

(a) a nucleic acid molecule that comprises an A for a G at position 1493 of SEQ ID NO:1447 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1447 contiguously appurtenant to said position; and  
(b) a nucleic acid which is fully complementary to a nucleic acid molecule of (a).

15 In this embodiment, the isolated nucleic acid molecule can be defined, in part, as comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 72, SEQ ID NO: 74, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID  
20 NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 98, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 150, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 160, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 168, SEQ ID NO: 170, SEQ ID NO: 172,  
25 SEQ ID NO: 205, SEQ ID NO: 207, SEQ ID NO: 209, SEQ ID NO: 211, SEQ ID NO: 213, SEQ ID NO: 215, SEQ ID NO: 217, SEQ ID NO: 219, SEQ ID NO: 249, SEQ ID NO: 251, SEQ ID NO: 253, SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 297, SEQ ID NO: 299, SEQ ID NO: 301, SEQ ID NO: 303, SEQ ID NO: 305, SEQ ID NO: 307, SEQ ID NO: 309, SEQ ID NO: 311, SEQ ID NO: 313, SEQ ID NO: 315, SEQ  
30 ID NO: 317, SEQ ID NO: 319, SEQ ID NO: 321, SEQ ID NO: 323, SEQ ID NO: 325, SEQ ID NO: 327, SEQ ID NO: 329, SEQ ID NO: 331, SEQ ID NO: 340, SEQ ID NO: 342, SEQ ID NO: 344, SEQ ID NO: 346, SEQ ID NO: 348, SEQ ID NO: 350, SEQ ID NO: 352, SEQ ID NO: 354, SEQ ID NO: 393, SEQ ID NO: 395, SEQ ID NO: 397, SEQ ID NO: 399, SEQ ID NO: 401, SEQ ID NO: 403, SEQ ID NO: 405, SEQ ID NO: 407, SEQ ID NO: 409, SEQ ID NO: 411, SEQ ID  
35 NO: 413, SEQ ID NO: 415, SEQ ID NO: 417, SEQ ID NO: 419, SEQ ID NO: 421, SEQ ID NO: 423, SEQ ID NO: 425, SEQ ID NO: 427, SEQ ID NO: 429, SEQ ID NO: 431, SEQ ID NO: 433,

SEQ ID NO: 435, SEQ ID NO: 437, SEQ ID NO: 439, SEQ ID NO: 441, SEQ ID NO: 443, SEQ ID NO: 445, SEQ ID NO: 447, SEQ ID NO: 449, SEQ ID NO: 451, SEQ ID NO: 453, SEQ ID NO: 455, SEQ ID NO: 457, SEQ ID NO: 459, SEQ ID NO: 461, SEQ ID NO: 463, SEQ ID NO: 465, SEQ ID NO: 467, SEQ ID NO: 469, SEQ ID NO: 471, SEQ ID NO: 506, SEQ ID NO: 508, 5 SEQ ID NO: 510, SEQ ID NO: 512, SEQ ID NO: 514, SEQ ID NO: 516, SEQ ID NO: 518, SEQ ID NO: 520, SEQ ID NO: 522, SEQ ID NO: 524, SEQ ID NO: 536, SEQ ID NO: 538, SEQ ID NO: 540, SEQ ID NO: 542, SEQ ID NO: 544, SEQ ID NO: 567, SEQ ID NO: 569, SEQ ID NO: 571, SEQ ID NO: 573, SEQ ID NO: 575, SEQ ID NO: 577, SEQ ID NO: 579, SEQ ID NO: 581, SEQ ID NO: 583, SEQ ID NO: 585, SEQ ID NO: 587, SEQ ID NO: 589, SEQ ID NO: 591, SEQ ID NO: 617, SEQ ID NO: 619, SEQ ID NO: 621, SEQ ID NO: 623, SEQ ID NO: 625, SEQ ID NO: 627, SEQ ID NO: 629, SEQ ID NO: 631, SEQ ID NO: 633, SEQ ID NO: 646, SEQ ID NO: 648, SEQ ID NO: 650, SEQ ID NO: 652, SEQ ID NO: 654, SEQ ID NO: 676, SEQ ID NO: 678, SEQ ID NO: 680, SEQ ID NO: 682, SEQ ID NO: 684, SEQ ID NO: 686, SEQ ID NO: 688, SEQ ID NO: 690, SEQ ID NO: 692, SEQ ID NO: 694, SEQ ID NO: 696, SEQ ID NO: 698, SEQ ID NO: 700, SEQ ID NO: 702, SEQ ID NO: 704, SEQ ID NO: 706, SEQ ID NO: 708, SEQ ID NO: 710, SEQ ID NO: 712, SEQ ID NO: 714, SEQ ID NO: 716, SEQ ID NO: 718, SEQ ID NO: 720, SEQ ID NO: 738, SEQ ID NO: 740, SEQ ID NO: 742, SEQ ID NO: 744, SEQ ID NO: 766, SEQ ID NO: 768, SEQ ID NO: 770, SEQ ID NO: 772, SEQ ID NO: 774, SEQ ID NO: 776, SEQ ID NO: 778, SEQ ID NO: 780, SEQ ID NO: 782, SEQ ID NO: 784, SEQ ID NO: 786, SEQ ID NO: 788, SEQ ID NO: 809, SEQ ID NO: 811, SEQ ID NO: 813, SEQ ID NO: 815, SEQ ID NO: 817, SEQ ID NO: 819, SEQ ID NO: 821, SEQ ID NO: 823, SEQ ID NO: 825, SEQ ID NO: 840, SEQ ID NO: 842, SEQ ID NO: 844, SEQ ID NO: 846, SEQ ID NO: 848, SEQ ID NO: 850, SEQ ID NO: 852, SEQ ID NO: 854, SEQ ID NO: 856, SEQ ID NO: 858, SEQ ID NO: 860, SEQ ID NO: 862, SEQ ID NO: 864, SEQ ID NO: 866, SEQ ID NO: 895, SEQ ID NO: 897, SEQ ID NO: 899, 25 SEQ ID NO: 901, SEQ ID NO: 903, SEQ ID NO: 905, SEQ ID NO: 907, SEQ ID NO: 909, SEQ ID NO: 911, SEQ ID NO: 913, SEQ ID NO: 915, SEQ ID NO: 917, SEQ ID NO: 982, SEQ ID NO: 984, SEQ ID NO: 986, SEQ ID NO: 988, SEQ ID NO: 990, SEQ ID NO: 992, SEQ ID NO: 994, SEQ ID NO: 996, SEQ ID NO: 998, SEQ ID NO: 1000, SEQ ID NO: 1002, SEQ ID NO: 1004, SEQ ID NO: 1006, SEQ ID NO: 1008, SEQ ID NO: 1010, SEQ ID NO: 1012, SEQ ID NO: 1014, SEQ ID NO: 1016, SEQ ID NO: 1018, SEQ ID NO: 1020, SEQ ID NO: 1022, SEQ ID NO: 1024, SEQ ID NO: 1026, SEQ ID NO: 1028, SEQ ID NO: 1030, SEQ ID NO: 1032, SEQ ID NO: 1034, SEQ ID NO: 1036, SEQ ID NO: 1038, SEQ ID NO: 1040, SEQ ID NO: 1042, SEQ ID NO: 1044, SEQ ID NO: 1046, SEQ ID NO: 1048, SEQ ID NO: 1050, SEQ ID NO: 1052, SEQ ID NO: 1054, SEQ ID NO: 1056, SEQ ID NO: 1058, SEQ ID NO: 1060, SEQ ID NO: 1062, SEQ ID NO: 1064, SEQ ID NO: 1121, SEQ ID NO: 1123, SEQ ID NO: 1125, SEQ ID NO: 1127, SEQ ID NO: 1129, SEQ ID NO: 1131, SEQ ID NO: 1133, SEQ ID NO: 1135, SEQ ID NO: 1137, SEQ ID NO:



1139, SEQ ID NO: 1141, SEQ ID NO: 1143, SEQ ID NO: 1145, SEQ ID NO: 1147, SEQ ID NO:  
 1149, SEQ ID NO: 1151, SEQ ID NO: 1153, SEQ ID NO: 1155, SEQ ID NO: 1157, SEQ ID NO:  
 1159, SEQ ID NO: 1161, SEQ ID NO: 1163, SEQ ID NO: 1165, SEQ ID NO: 1167, SEQ ID NO:  
 1169, SEQ ID NO: 1171, SEQ ID NO: 1173, SEQ ID NO: 1175, SEQ ID NO: 1177, SEQ ID NO:  
 5 1179, SEQ ID NO: 1181, SEQ ID NO: 1183, SEQ ID NO: 1185, SEQ ID NO: 1187, SEQ ID NO:  
 1189, SEQ ID NO: 1191, SEQ ID NO: 1193, SEQ ID NO: 1195, SEQ ID NO: 1197, SEQ ID NO:  
 1199, SEQ ID NO: 1201, SEQ ID NO: 1262, SEQ ID NO: 1264, SEQ ID NO: 1266, SEQ ID NO:  
 1268, SEQ ID NO: 1270, SEQ ID NO: 1272, SEQ ID NO: 1274, SEQ ID NO: 1276, SEQ ID NO:  
 1278, SEQ ID NO: 1280, SEQ ID NO: 1282, SEQ ID NO: 1284, SEQ ID NO: 1286, SEQ ID NO:  
 10 1288, SEQ ID NO: 1290, SEQ ID NO: 1292, SEQ ID NO: 1294, SEQ ID NO: 1296, SEQ ID NO:  
 1298, SEQ ID NO: 1300, SEQ ID NO: 1302, SEQ ID NO: 1304, SEQ ID NO: 1306, SEQ ID NO:  
 1308, SEQ ID NO: 1310, SEQ ID NO: 1312, SEQ ID NO: 1314, SEQ ID NO: 1316, SEQ ID NO:  
 1318, SEQ ID NO: 1320, SEQ ID NO: 1322, SEQ ID NO: 1346, SEQ ID NO: 1348, SEQ ID NO:  
 1350, SEQ ID NO: 1352, SEQ ID NO: 1354, SEQ ID NO: 1356, SEQ ID NO: 1358, SEQ ID NO:  
 15 1360, SEQ ID NO: 1362, SEQ ID NO: 1364, SEQ ID NO: 1366, SEQ ID NO: 1368, SEQ ID NO:  
 1370, SEQ ID NO: 1372, SEQ ID NO: 1374, SEQ ID NO: 1376, SEQ ID NO: 1390, SEQ ID NO:  
 1392, SEQ ID NO: 1394, SEQ ID NO: 1401, SEQ ID NO: 1418, SEQ ID NO: 1420, SEQ ID NO:  
 1422, SEQ ID NO: 1424, SEQ ID NO: 1426, SEQ ID NO: 1435, SEQ ID NO: 1437, SEQ ID NO:  
 1439, and SEQ ID NO: 1446.

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The present invention also includes nucleic acid molecules that are oligonucleotides capable of hybridizing, under stringent hybridization conditions, with complementary regions of a CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA,  
 25 MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 gene or other CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 nucleic acid molecule containing a polymorphism of the present invention. Oligonucleotides of the present  
 30 invention can be RNA, DNA, or derivatives of either. The minimum size of such oligonucleotides is the size required for formation of a stable hybrid between an oligonucleotide and a complementary sequence on a nucleic acid molecule of the present invention. Minimal size characteristics are disclosed herein. The present invention includes oligonucleotides that can be used as, for example, probes to identify nucleic acid molecules or primers to produce nucleic acid  
 35 molecules. Also provided are oligonucleotides that can be used as primers to amplify DNA. Preferred oligonucleotide probes or primers include a single base change of a polymorphism of

the present invention or the wildtype nucleotide that is located at the same position. Preferably the nucleotide of interest occupies a central position of a probe. Preferably the nucleotide of interest occupies a 3' position of a primer.

The minimal size of an oligonucleotide of the present invention is typically at least about 5 15 to about 18 bases in length. Unless specified otherwise, there is no limit, other than a practical limit, on the maximal size of such a nucleic acid molecule in that the nucleic acid molecule can include a portion of a gene, an entire gene, multiple genes, or portions thereof. In preferred embodiments, however, nucleic acid molecules of the present invention are typically less than about 5 kilobases in length and more preferably less than about 70 nucleotides in length. For 10 instance, the present invention includes human CYP4501A1 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:31 or GenBank Accession No. X04300, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range 15 of 10-10,000.

The present invention includes human CYP1A2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:85-88 or GenBank Accession No. M31664, M31665, M31666, M31667, or U02993, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 20 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CYP4502E1 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:111 or GenBank Accession No. D10014, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 25 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human ADRB1 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:132 or GenBank Accession No. J03019, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 30 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human AHR alleles that comprise base changes as 35 described herein, having appurtenant sequences, based on either SEQ ID NOs:173-177 or GenBank Accession No. D31708, U27657, U28060, D38044, L19872, U28064, U28065, of 10,

15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human ARNT alleles that comprise base changes as  
5 described herein, having appurtenant sequences, based on SEQ ID NOs:220-234, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CTSS alleles that comprise base changes as  
10 described herein, having appurtenant sequences, based on either SEQ ID NOS:264-269 or GenBank Accession No. U07369, U07370, U073671, U07372, or U073674, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

15 The present invention includes human COX2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:332 or GenBank Accession No. U04636, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range  
20 of 10-10,000.

The present invention includes human DBI alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:355 or GenBank Accession No. X94563, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195,  
25 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human EPHX2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:472-486 or GenBank Accession No. X97024, X97025, X97026, X97027, X97028, X97029, X97030,  
30 X97031, X97032, X97033, X97034, X97035, X97036, X97037, or X97038, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human FLAP alleles that comprise base changes as  
35 described herein, having appurtenant sequences, based on either SEQ ID NOs:525-528 or GenBank Accession No. M60470, M63259, M63260, or M63261, of 10, 15, 20, 25, 30, 35, 45, 50,

55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human GST12 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:545-547 or GenBank Accession No. U46495, U46498, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

10 The present invention includes human HNMT alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:592-597 or GenBank Accession No. U441106, U441107, U441108, U44109, U44110, U44111, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human KLK2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:635 or GenBank Accession No. M18157, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human NNMT alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:655 AND 656 or GenBank Accession No. U20970 or U20971, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human NQO2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:721-727, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human STM alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:745 or GenBank Accession No. U20499, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195,

200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human UGT2B7 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:826, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human UGT2B15 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:867, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human uPA alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO: 918 or GenBank Accession No. X02419, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human MDR1 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1065-1067 or GenBank Accession No. AC002457, M57450, or AC005068, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human LTF alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:1202-1216 or GenBank Accession No. AC002457, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human MRP3 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1322 or GenBank Accession No. AC004590, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human NR1I2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NOs:1377-1381, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CHMR1 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1394 or GenBank Accession No. Y00508/M35128, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CHMR2 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1401 or GenBank Accession No. M16404, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CHMR3 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1426 or GenBank Accession No. U29589, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CHMR4 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1439 or GenBank Accession No. M16405, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

The present invention includes human CHMR5 alleles that comprise base changes as described herein, having appurtenant sequences, based on either SEQ ID NO:1446 or GenBank Accession No. M80333, of 10, 15, 20, 25, 30, 35, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 250, 300, 350, 400, 450, 500, or 1000 bases, or any whole number encompassed by the range of 10-10,000.

In various embodiments of the foregoing descriptions of nucleic acid molecules of the present invention, the nucleic acid molecule can include one or more polymorphism for any particular gene. However, in other embodiments, such as nucleic acid molecules which are useful in linkage analysis, the nucleic acid molecules have one and only one identified polymorphism.

5 In various embodiments of the foregoing descriptions of nucleic acid molecules of the present invention, the nucleic acid molecule can include an entire coding sequence from a particular gene, such that expression of the nucleic acid molecule produces a full length protein. Such full length proteins can be either functional or non-functional depending on the polymorphism in question. Assays for testing functionality for the various proteins described  
10 herein are well-known in the art.

As used herein, hybridization conditions refer to standard hybridization conditions under which nucleic acid molecules are used to identify similar nucleic acid molecules. Such standard conditions are disclosed, for example, in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press, 1989. Sambrook et al., *ibid.*, is incorporated by  
15 reference herein in its entirety (see specifically, pages 9.31-9.62). In addition, formulae to calculate the appropriate hybridization and wash conditions to achieve hybridization permitting varying degrees of mismatch (e.g., 80%, 85%, 90%, 95%, or 98%) of nucleotides are disclosed, for example, in Meinkoth et al., 1984, *Anal. Biochem.* 138, 267-284; Meinkoth et al., *ibid.*, is incorporated by reference herein in its entirety.

20 The genotype of an individual is determined with respect to the provided CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, and/or CHMR5 gene polymorphisms. The genotype is useful for determining the presence of phenotypically evident polymorphism, and for  
25 determining the linkage of a polymorphism to a phenotypic change.

One embodiment of the present invention is a method of identifying a sample containing a nucleic acid molecule that comprises a wildtype or variant allele, the method comprising identifying the presence or absence of one or more polymorphisms in a sequence of a gene that is capable of encoding CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS,  
30 COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 protein.

Another embodiment of the present invention is a method for identifying whether a sample containing a nucleic acid molecule is associated with altered drug metabolism or  
35 susceptibility to cancer, the method comprising identifying the presence or absence of one or more CYP4501A1, CYP4501A2, AHR, MDR1, MDR3, CYP4502E1, ARNT, EPHX, GST12, NNMT,

NQO2, NR1I2, STM, UGT2B4, UGT2B7 and/or UGT2B15 alleles, wherein the pattern of alleles is indicative of altered drug metabolism or susceptibility to cancer.

Another embodiment of the present invention is a method of identifying a sample containing a nucleic acid molecule that is associated with altered pulmonary or cardiovascular function, the method comprising identifying the presence or absence of a polymorphism in the nucleic acid sequence encoding ADRB1, CHRM2 or CTSS protein, wherein said polymorphism is indicative of pulmonary or cardiovascular function.

The invention provides a variety of assays for identifying individuals having one or more wildtype or variant alleles. The assays identify polymorphisms of the present invention in CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, and/or CHMR5 cDNA or genomic DNA (i.e., including the entire CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 gene and not just the coding region). Such assays are referred to herein as "cDNA assays" and "genomic DNA assays." It should be noted that genomic DNA assays include not only analysis of actual genomic DNA derived from a natural source, but also analysis of any amplification product or other derivative (e.g., restriction fragments) of genomic DNA derived from a natural source. The cDNA assays are particularly useful for de novo localization of a CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 polymorphism to a particular nucleotide or nucleotides. The genomic assays are particularly useful for rapid screening of individuals for the presence of a polymorphism.

Many of the diagnostic assays rely on amplification of part or all of a CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 nucleic acid molecule. In one embodiment, portions of a CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 nucleic acid molecule are amplified by the polymerase chain reaction (PCR). The PCR process is described in e.g., U.S. Pat. Nos. 4,683,195; 4,683,202; and 4,965,188; PCR Technology: Principles and Applications for DNA Amplification (ed. Erlich, Freeman Press, New York, N.Y., 1992); PCR Protocols: A Guide to Methods and Applications (eds. Innis et al.,



Academic Press, San Diego, Calif. (1990); Mattila et al. Nucleic Acids Res. 19:4967 (1991); Eckert & Kunkel PCR Methods and Applications 1:17 (1991); PCR (eds. McPherson et al., IRL Press, Oxford), each of which is incorporated by this reference in its entirety.

To amplify a portion of a CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 nucleic acid molecule in a sample by PCR, the sequence must be accessible to the components of the amplification system. Accessibility can be achieved by isolating nucleic acid molecules from the sample. A variety of techniques for extracting nucleic acid molecules from biological samples are known in the art. Alternatively, if the sample is readily disruptable, the nucleic acid need not be purified prior to amplification by the PCR technique, i.e., if the sample comprises cells, particularly peripheral blood lymphocytes or monocytes, lysis and dispersion of the intracellular components may be accomplished merely by suspending the cells in hypotonic buffer. See Han *et al.*, Biochemistry, 1987, vol. 26, pages 1617-1625. Polymorphisms are detected in a nucleic acid molecule from an individual being analyzed. For assay of genomic DNA, virtually any biological sample (other than pure red blood cells) is suitable. Examples of convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair. Nucleic acid molecules can be obtained according to procedures well-known in the art.

For amplification of mRNA sequences, a cDNA template is first produced by reverse transcription. Reverse transcription is the polymerization of deoxynucleoside triphosphates to form primer extension products that are complementary to a ribonucleic acid template. The process is effected by reverse transcriptase, an enzyme that initiates synthesis at the 3'-end of the primer and proceeds toward the 5'-end of the template until synthesis terminates. Examples of suitable polymerizing agents that convert the RNA nucleic acid molecule into a complementary cDNA sequence are avian myeloblastosis virus reverse transcriptase and *Thermus thermophilus* DNA polymerase. Reverse transcription can be carried out as a separate step, or in a homogeneous reverse transcription-polymerase chain reaction (RT-PCR). Polymerizing agents suitable for synthesizing a cDNA sequence from the RNA template are reverse transcriptase (RT), such as avian myeloblastosis virus RT, Moloney murine leukemia virus RT, or *Thermus thermophilus* DNA polymerase.

Primers for PCR amplification are designed so that the position at which each primer hybridizes along a duplex sequence is such that an extension product synthesized from one primer, when separated from the template (complement), serves as a template for the extension of the other primer. The primers are selected to be substantially complementary to the different strands of each specific sequence to be amplified. This means that the primers must be sufficiently

complementary to hybridize with their respective strands. Therefore, the primer sequence need not reflect the exact sequence of the template. For example, a non-complementary nucleotide fragment may be attached to the 5' end of the primer with the remainder of the primer sequence being complementary to the strand. Alternatively, complementary bases or longer sequences can be interspersed into the primer, provided that the primer sequence has sufficient complementarity with the sequence of the strand to be amplified to hybridize therewith and thereby form a template for synthesis of the extension product of the other primer. Paired primers for amplification of a given segment of DNA are designated forward and reverse primers. The forward primer hybridizes to a double-stranded DNA molecule at a position 5', or upstream, from the reverse primer. The forward primer hybridizes to the complement of the coding strand of the double stranded sequence, i.e., the antisense strand, and the reverse primer hybridizes to the coding strand.

The appropriate length of a primer depends on the intended use of the primer but typically ranges from about 10 to about 100, preferably about 15 to about 50, more preferably about 15 to about 35, or more preferably about 20 to about 30 nucleotides in length. The spacing of primers determines the length of segment to be amplified. The spacing is not usually critical and amplified segments can range in size from about 25 bases to at least about 35 kilobases in length. Segments from about 25 to about 2000, preferably about 50 to about 1000, more preferably about 100 to about 500 nucleotides in length are typical.

A primer can be labeled, if desired, by incorporating a label detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include  $^{32}\text{P}$ , fluorescent dyes, electron-dense reagents, enzymes (as commonly used in an ELISA), biotin, or haptens and proteins for which antisera or monoclonal antibodies are available. A label can also be used to "capture" the primer, so as to facilitate the immobilization of either the primer or a primer extension product, such as amplified DNA, on a solid support.

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics*, 1989, vol. 4, pages 560-569; Landegren *et al.*, *Science*, 1988, vol. 241, pages 1077-1080; transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA*, 1989, vol. 86, pages 1173-1177), and self-sustained sequence replication (Guatelli *et al.*, *Proc. Nat. Acad. Sci. USA*, 1990, vol. 87, pages 1874-1878) and nucleic acid based sequence amplification (NASBA). The latter two amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

An allele-specific primer can be used in PCR amplification reactions. The allele-specific primer hybridizes to a site on a nucleic acid molecule that overlaps with a polymorphism and extension will only occur if an allelic form complementary to the primer is present. See Gibbs,

Nucleic Acid Res., 1989, vol. 17, pages 2427-2448. This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers leading to a detectable product signifying the particular allelic form is present. Thus, the presence or absence of an amplification product is detected using standard methods. Controls can be used  
5 that test the efficacy of the amplification reaction itself or that allow the experimental results to be compared with known wildtype or polymorphic CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 [WHERE IS CHMR5? ARE ALL THESE LISTS  
10 THROUGHOUT THE PATENT COMPLETE?-ALL OF THE OTHER LISTS WERE CHECKED AND HAD ALL 30 GENES REFERENCED] nucleic acid molecule samples. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer.

15 Sample nucleic acid molecules, isolated directly from cells, amplified or cloned fragments, can also be analyzed by a number of other methods known in the art. The nucleic acid molecule can be sequenced by using either the dideoxy chain termination method or other methods (see for example Sambrook *et al.*, Molecular Cloning, A Laboratory Manual (2nd Ed., CSHP, New York 1989); Zyskind *et al.*, Recombinant DNA Laboratory Manual, (Acad. Press,  
20 1988)).

Hybridization using allele-specific probes, described by e.g., Saiki *et al.*, Nature 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548, can be used to determine the presence or absence of a polymorphism by, for example Southern blot, dot blots, etc. An allele-specific probe can be designed that hybridizes to a segment of a nucleic acid molecule from one individual  
25 but does not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles.

The hybridization pattern of a control and variant sequence to an array of oligonucleotide  
30 probes immobilized on a solid support, as described in US Pat. No. 5,445,934, or in WO 95/35505, can also be used as a means of detecting the presence of variant sequences.

Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis (DGGE). Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of  
35 DNA in solution. Erlich, ed., PCR Technology, Principles and Applications for DNA Amplification, (W.H. Freeman and Co, New York, 1992), Chapter 7.

Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis (SSCP), which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, Proc. Nat. Acad. Sci. 86, 2766-2770 (1989). Amplified PCR products can be generated as described above, and heated or  
5 otherwise denatured, to form single stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence difference between alleles of target sequences.

Other methods of detection include mismatch cleavage detection and heteroduplex  
10 analysis in gel matrices. These methods are used to detect conformational changes created by DNA sequence variation as alterations in electrophoretic mobility. Alternatively, where a polymorphism creates or destroys a recognition site for a restriction endonuclease, referred to as restriction length polymorphism, or RFLP, the sample is digested with that endonuclease and the products size fractionated to determine whether the fragment was digested. Fractionation is  
15 performed by gel or capillary electrophoresis, particularly acrylamide or agarose gels.

In one embodiment of the present invention, an array of oligonucleotides are provided, where discrete positions on the array are complementary to one or more of the provided polymorphic sequences, e.g. oligonucleotides of at least 12 nucleotides, frequently 20 nucleotides or larger and including the sequence flanking the polymorphic position. Such an array may  
20 comprise a series of oligonucleotides, each of which can specifically hybridize to a different polymorphism. For examples of arrays, see Hacia *et al.*, 1996, Nat. Genet., vol. 14, pages 441-447 and DeRisi *et al.*, 1996, Nat. Genet., vol. 14, pages 457-460. Arrays of interest may further comprise sequences, including polymorphisms, of other genetic sequences, particularly other sequences of interest for pharmacogenetic screening.

It is within the scope of the present invention that one or more CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 polymorphisms provided herein can be  
25 detected in a single assay such as a multiplex assay to identify the presence or absence of different alleles in the same assay, see for example Stuvén *et al.*, Pharmacogenetics, 1996, vol. 6, pages 417-421.

One embodiment of the present invention is a diagnostic kit. The kit comprises useful components for practicing the methods of the present invention. The kit typically comprises at least one of the primers needed for the PCR amplification if PCR amplification is used and also  
35 control DNA suitable for determining the success of the PCR reaction and/or to confirm the identification of the presence or absence of a polymorphism in a sample. A kit usually contains a

matched pair of forward and reverse primers as described above for amplifying a segment encompassing a polymorphism of the present invention. For selective amplification of mutant or wildtype alleles, kits usually contain a pair of primers for amplification of the mutant allele and/or a separate pair of primers for amplification of the wildtype allele. Optional additional components of the kit include, for example, restriction enzymes for analysis of amplification products, reverse-transcriptase or polymerase, the substrate nucleoside triphosphates, and the appropriate buffers for reverse transcription, PCR, or restriction enzyme reactions. Usually, the kit also contains instructions for carrying out the methods.

The method of the present invention is characterized by detecting the polymorphisms provided herein, and is useful in gene diagnosis for detecting CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, and/or CHMR5 gene polymorphisms. As long as the method is capable of detecting the aforementioned specific types of mutation which are clearly defined and characterized by the present invention, no limitation is imposed on the technique, etc. to be employed in the method. For example, a variety of routine methods may be widely used. Since the types of gene mutation to be detected by the present invention are now clarified and specified, it would be obvious for skilled persons in the art to adopt a suitable method for detecting them from the reading of the disclosure of this specification.

Also provided by the present invention are methods for detecting a polymorphic sequence of the CYP4501A1, CYP4501A2, CYP4502E1, ADRB1, AHR, ARNT, CTSS, COX2, DBI, EPHX2, FLAP, GST12, HNMT, KLK2, NNMT, NQO2, STM, UGT2B4, UGT2B7, UGT2B15, uPA, MDR1, LTF, MRP3, NR1I2, CHMR1, CHMR2, CHMR3, CHMR4, or CHMR5 gene in a sample containing human nucleic acid molecules comprising identifying the presence or absence of one of the newly identified polymorphisms of the present invention in any of the human nucleic acid molecules.

In one embodiment, said method further comprises: (a) mixing said nucleic acid molecules with one or more second nucleic acid molecules of the present invention so as to form a mixture; (b) subjecting said mixture to hybridization conditions; and (c) detecting any hybrids formed. Those methods wherein said nucleic acid is amplified prior to step (a) are preferred. The materials useful for these methods can be obtained as described, and these methods can be accomplished as discussed. In a preferred embodiment, the second nucleic acid molecule consists of a primer of the present invention and step (c) is accomplished by determining the presence or absence of a PCR product. In another preferred embodiment, the second nucleic acid molecule is a probe of the present invention, wherein the probe is labeled with a detectable marker and step (c) is accomplished by determining the presence or absence of the detectable marker.

In other embodiments, methods of the present invention comprise digesting DNA comprising at least a part of the nucleic acid sequence containing the polymorphic site with a restriction enzyme that will cut, or will not cut, at or adjacent to one of the polymorphic positions according to whether the polymorphism is present. In this manner, such restriction enzymes distinguish between wildtype and mutant alleles. Those methods wherein said nucleic acid is amplified prior to the digestion step are preferred. The materials useful for these methods can be obtained as described, and these methods can be accomplished as discussed.

Polyclonal and/or monoclonal antibodies that specifically bind to variant gene products but not to corresponding prototypical gene products are also provided. Antibodies can be made by injecting mice or other animals with the variant gene product or synthetic peptide fragments thereof. Monoclonal antibodies are screened as are described, for example, in Harlow & Lane, *Antibodies, A Laboratory Manual*, Cold Spring Harbor Press, New York (1988); Goding, *Monoclonal antibodies, Principles and Practice* (2d ed.) Academic Press, New York (1986). Monoclonal antibodies are tested for specific immunoreactivity with a variant gene product and lack of immunoreactivity to the corresponding prototypical gene product. These antibodies are useful in diagnostic assays for detection of the variant form, or as an active ingredient in a pharmaceutical composition.

Another embodiment of the present invention includes a computer for displaying a nucleic acid sequence of a molecule of the present invention, as broadly described herein. Such a computer includes a computer-readable medium encoded with one or more of said nucleic acid sequences to create an electronic file. The computer further includes hardware and software that display the nucleic acid sequence in the electronic file as a linear model of the molecule for analysis, alignment with other sequences or visualization of the nucleic acid sequence by the computer. Such hardware and software components are well-known in the art. Also provided are databases comprising sequence information pertaining to nucleic acid molecules of the present invention.

The following Examples are provided to illustrate embodiments of the present invention and are not intended to limit the scope of the invention as set forth in the claims.

#### Example 1

This example describes the identification of variants of the known cytochrome P450 1A1 sequence (CYP4501A1).

Blood specimens from 32 individuals were collected after obtaining informed consent. All samples were stripped of personal identifiers to maintain confidentiality. The only data associated with each sample was self-reported gender and racial group designations. Of the 32 individuals, 10 were African Americans, 10 were Caucasians, 6

were Japanese and 6 were Chinese. Genomic DNA was isolated using standard methods. Polymerase chain reaction (PCR) amplification of regions of the CYP4501A1 gene was performed using the primers listed in Table 1. Each PCR amplification was performed in a total reaction volume of 100 microliters ( $\mu$ l). The final magnesium chloride concentration for each reaction was optimized empirically as shown in Table 1. The final genomic DNA concentration was about 100 nanogram (ng) per reaction from 2 individuals. The PCR reactions were performed using Perkin Elmer's GeneAmp® PCR kit (available from Perkin Elmer, Norwalk, CN) using Taq Gold® DNA polymerase according to manufacturer's instructions and using the following primers.

**Table 1. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'	[Mg <sup>++</sup> ]
Promoter 1A	F	1	CCATCAGAATGTAAACTCCAC	1mM
Promoter 1A	R	2	TCCTCGCAGCCTCT	1mM
Promoter 1B	F	3	GGATTCTGTGCTCTGC	1mM
Promoter 1B	R	4	GCTAGACTGCCTGGTC	1mM

Thermal cycling was performed using a GeneAmp® PCR System 9600 PCR machine (available from Perkin Elmer) with an initial denaturation step at 95°C for 10 min, followed by 35 cycles for promoter 1A or 40 cycles for promoter 1B of;

denaturation at 95°C for 30 sec,

primer annealing at 55°C for promoter 1A or 60°C for promoter 1B for 45 sec, and

primer extension at 72°C for 2 min;

followed by final extension at 72°C for 5 min.

The resulting PCR products were purified using Microcon-100® columns (available from Millipore, Bedford, MA). PCR products from two individuals were combined for each cycle of sequencing. Cycle sequencing was performed on the GeneAmp® PCR System 9600 PCR machine using the ABI Prism dRhodamine Terminator Cycle Sequencing Ready Reaction Kit® (available from Applied Biosystems, Inc., Foster City, CA) according to the manufacturer's directions. Oligonucleotide primers used for the sequencing reactions include SEQ ID NO:1 and those shown in Table 2.

Table 2. Sequencing Primers

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter 1A	F	5	TCCTGGAAACCCTGT
5 Promoter 1A	F	6	GTCCTTCTCACGCAAC
Promoter 1A	R	7	GGAAAAAAAAAAGTTGTATTTC
Promoter 1A	R	8	CGATTGAATAAGGGGATG
Promoter 1A	R	9	AGCCCCCACCCTACC
Promoter 1A	R	10	GCCTTAGTGCTGATTGC
10 Promoter 1B	F	11	GCCAATCAAAGCACTAGC
Promoter 1B	R	12	CAGGACAGCCCGAAG

About 8 µl sequencing reactions were subjected to 30 cycles at 96°C for 20 sec, 50°C for 20 sec, and 60°C for 4 min, followed by ethanol precipitation. Samples were evaporated to dryness at 50°C for about 15 min and resuspended in 2 µl of loading buffer (5:1 deionized formamide:50 mM EDTA pH 8.0), heated to 65°C for 5 min, and electrophoresed through 4% polyacrylamide/6M urea gels in an ABI 377 Nucleic Acid Analyzer according to the manufacturer's instructions to obtain sequence information. All sequences were determined in both the 5' and 3' (sense and antisense) directions. The 16 electropherograms were analyzed by comparing peak heights, looking for about 25% reduction in peak size and/or the presence of extra peaks as an indication of heterozygosity.

Polymorphic sequences identified from the sequencing are shown below the wildtype sequence, both of which are shown in bold, and listed below in Table 3. For example, a variation of a T to an A was discovered at base pair -1603 in the promoter region of the CYP4501A1 gene.

Table 3. Newly Identified CYP4501A1 Gene Polymorphisms

Location	SEQ ID NO	Polymorphism Sequence
Promoter; -1602	13	TCAGCTGTGTTCCCTTCTCTG
30	14	TCAGCTGTGTACCCCTTCTCTG
Promoter; -1579	15	AATCGCCAGCACCTCCGAACA
	16	AATCGCCAGCGCCTCCGAACA
Promoter; -1315	17	GGACAGCGTCGGAGGCAGGCA
	18	GGACAGCGTCAGAGGCAGGCA
35 Promoter; -1060	19	TCCCTCCCCCTCGCGTGACT
	20	TCCCTCCCCCGTCGCGTGACT
Promoter; -1034	21	CCCCCGCGCCGGCCGGGGAA



		100	
	22	CCCCCGCGCCAGGCCGGGGAA	
Promoter; -1019	23	GGGGAATGGGTCTGGCTGGGTG	
	24	GGGGAATGGGGCGGCTGGGTG	
Promoter; -976	25	CTCACGCAACGCCTGGGCACC	
5	26	CTCACGCAACTCCTGGGCACC	
Promoter; -946	27	GGCCAGGTGGGGCGGGGACGG	
	28	GGCCAGGTGGAGCGGGGACGG	
Promoter; -468	29	CCCCGGGAAGGAGGTCACCAC	
	30	CCCCGGGAAGAAGGTCACCAC	
10	SEQ ID NO:31 lists the sequence of the reference CYP4501A1 gene (GenBank Accession No. X04300).		

### Example 2

This example describes the identification of variants of the known cytochrome P450 1A2 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the CYP4501A2 gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 4. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

20

**Table 4. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'	[Mg <sup>++</sup> ]
Promoter 1A	F	32	AGGTACAGAATGGAAAGGTG	1.5mM
25 Promoter 1A	R	33	GGAAGGGGAATCCAAT	1.5mM
Promoter 1B	F	34	ATCTGAACCCAATGGAG	1mM
Promoter 1B	R	35	TGATCCCCACAACCTC	1mM
Promoter 1C	F	36	TAGAGACGGAGTTTCACCAG	1.5mM
Promoter 1C	R	37	GGAAACAGAAGTCAAGAGC	1.5mM
30 Exon 2	F	38	ATCTTGAGGCTCCTTTCC	1.5mM
Exon 2	R	39	AGAGTCGGCTCCAGGT	1.5mM
Exon 3	F	40	AAAATGACACTTTAAGCCATA	2mM
Exon 3	R	41	ATCTGATGTAGGGTTGGTG	2mM
Exon 4 and 5	F	42	TCAGTTTATGTTGAAGAGACC	2mM
35 Exon 4 and 5	R	43	GGGTTAGATTATGTTTGGG	2mM
Exon 6	F	44	CCCTCCCCTCCAGT	1mM
Exon 6	R	45	GCCATCCTAGTTGATTCC	1mM

101				
Exon 7	F	46	G TTCAGTTTGGTTCCTTC	2mM
Exon 7	R	47	GGTCCCACTATGTTGG	2mM

Thermal cycling was performed with an initial denaturation step at 95°C for 10 min, followed by 35 cycles of amplification for promoter 1A, promoter 1C, exons 2, 3, 4, 5, and 7 or 40 cycles of amplification for promoter 1B, and exon 6. Amplification consisted of denaturation at 95°C for 30 sec, annealing at 55°C for promoter 1A, promoter 1B, exon 3, 4, 5 or 7, 58°C for exon 6 or 60°C for promoter 1C or exon 2, for 45 sec, and primer extension at 72°C for 2 min, followed by final extension at 72°C for 5 min.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the sequences SEQ ID NOs:33, 40, 41, 44 or 45 and those shown in Table 5.

**Table 5. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter 1A	F	48	ACTTTACAGTGAAGAGACCTGA
Promoter 1B	F	49	CACCTGTGATTGTGGTC
Promoter 1B	R	50	AAAAAAAAAAAAATGTTACCTT
Promoter 1C	F	51	GCTGGTCTTGAACACCT
Promoter 1C	R	52	GGAGATTAGATGATATTCTGG
Exon 2	F	53	GCTTAGTCTTTCTGGTATCC
Exon 2	R	54	GGAGGTGTAGAGGTCAGG
Exon 4 and 5	F	55	CTTCAGGAAACTCACAGG
Exon 4 and 5	F	56	TGGGCTCACAGTAGTGC
Exon 4 and 5	R	57	GACTGTCTATCACAATCTGC
Exon 4 and 5	R	58	GGGGGCAGACTGAGG
Exon 7	F	59	CTGACCCCCATCTACG
Exon 7	R	60	TGGGCTCAAATGATCC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 6.

**Table 6. Newly Identified CYP4501A2 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence	Change
Promoter; -2216	61	CCAAAGAGACGTGATGACTAA	

		102	
	62	CCAAAGAGACATGATGACTAA	
Promoter; -1570	63	TTGTGGCACATGAACCCCAAC	
	64	TTGTGGCACAGAACCCCAAC	DEL T
Promoter; -906	65	TGATCCGCCCATCTCGGCCTC	
5	66	TGATCCGCCCCTCTCGGCCTC	
Promoter; -810	67	AAGGAGGTTGTGGGGATCATG	
	68	AAGGAGGTTGCGGGGATCATG	
Intron 1; 821	69	GGTCCCTCCTTTTTCCCTGCA	
	70	GGTCCCTCCTGTTTTCCCTGCA	
10 Exon 2; 62 (AA 18)	71	CTCCTGGCCTCTGCCATCTTC	
	72	CTCCTGGCCTGTGCCATCTTC	SER-
CYS			
Intron 2; 525	73	GGAGGATAGGGGGGTACCCAG	
	74	GGAGGATAGGAGGGTACCCAG	
15 Exon 3; 63 (AA 298)	75	CTAGAGCCAGCGGCAACCTCA	
	76	CTAGAGCCAGAGGCAACCTCA	SER-
ARG			
Intron 4; 43	77	GAAGCCTTGAAACCCAGGTTG	
	78	GAAGCCTTGAGACCCAGGTTG	
20 Intron 4; 201	79	ATGGGGTATAGAGGGGTATTC	
	80	ATGGGGTATACAGGGGTATTC	
Intron 6; 81	81	GAACTGTTTATATAATGAAAGGA	
	82	GAACTGTTTACATAATGAAAGGA	
Exon 7; 292	83	TCTCCATCAATTGAAGAAGAC	
25	84	TCTCCATCAACTGAAGAAGAC	

SEQ ID NO:85 lists the sequence of the reference CYP4501A2 gene (GenBank Accession No. M31664 and U02993), 5' flanking region and exons 1 and 2; SEQ ID NO:86 (GenBank Accession No. M31665), exons 3 through 5; SEQ ID NO:87 (GenBank Accession No. M31666), exon 6; and SEQ ID NO:88 (GenBank Accession No. M31667), exon 7.

### Example 3

This example describes the identification of variants of the known cytochrome P450 2E1 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the cytochrome P450 2E1

(CYP4502E1) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 7. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 7. PCR Primers and Mg<sup>++</sup> Concentration**

5	Region	Forward/ Reverse	SEQ ID NO:	5'-3'	[Mg <sup>++</sup> ]
	Promoter 1A	F	89	CTAACCCACCCGTGAGCCA	1.5mM
	Promoter 1A	R	90	TGATCCCGGCGCACAATAGA	1.5mM
	Promoter 1B	F	91	AGAGGCTGTTGCACCAGGAG	1.5mM
10	Promoter 1B	R	92	GGACACCAGCAGGAGGAAG	1.5mM

Thermal cycling was performed with an initial denaturation step at 95°C for 10 min, followed by 30 cycles of denaturation at 95°C for 30 sec, primer annealing at 55°C for 45 sec, and primer extension at 72°C for 2 min, followed by final extension at 72°C for 5 min.

- 15 The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used are shown in Table 8.

**Table 8. Sequencing Primers**

20	Region	Forward/ Reverse	SEQ ID NO:	5'-3'
	Promoter 1A	F	93	AGCCAGTCGAGTCTACAT
	Promoter 1A	R	94	ACCTCCACATTGACTAGC
	Promoter 1B	F	95	TACCGTGTCTAGAGGTGG
25	Promoter 1B	R	96	AAGGCCGCCCACACCAGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 9.

**Table 9. Newly Identified CYP4502E1 Gene Polymorphisms**

30	Location	SEQ ID NO	Polymorphism Sequence
	Promoter; -969	97	CAGTTAGAAGACAGAATGAAA
		98	CAGTTAGAAGGCAGAATGAAA
	Promoter; -894	99	GACTACCTTCATAGAAGGTGG
		100	GACTACCTTCGTAGAAGGTGG
35	Promoter; -376	101	TGGAGTTGTATTACATAAACC

		104	
	Promoter; -326	102	TGGAGTTGTAACATAAAACC
		103	CTGGAGTTCCCCGTTGTCTAA
		104	CTGGAGTTCCTCGTTGTCTAA
	Promoter; -316	105	CCGTTGTCTAACCAGTGCCAA
5		106	CCGTTGTCTAGCCAGTGCCAA
	Promoter; -299	107	CCAAAGGGCAGGTCGGTACCT
		108	CCAAAGGGCACGTCGGTACCT
	Promoter; -297	109	AAAGGGCAGGTCGGTACCTCA
		110	AAAGGGCAGGACGGTACCTCA
10	SEQ ID NO:111 lists the sequence of the reference CYP4502E1 gene (GenBank Accession No. D10014), promoter region and a portion of exon 1.		

#### Example 4

This example describes the identification of variants of the known  
15 adrenergic receptor B1 sequence.

Using genomic DNA samples obtained from different individuals as the  
initial template, PCR amplification of regions of the adrenergic receptor B1  
(ADRB1) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed  
in Table 10. PCR amplification reactions were generally performed as described  
20 in Example 1 using the following primers:

**Table 10. PCR Primers and Mg<sup>++</sup> Concentration**

	Region	Forward/ Reverse	SEQ ID NO:	5'-3'	[Mg <sup>++</sup> ]
25	Exon 1A	F	112	GGGCTTCTGGGGTGT	.75mM
	Exon 1A	R	113	CCACGATCACCAGCAC	.75mM
	Exon 1B	F	114	TGTGCTGGTGATCGTG	1mM
	Exon 1B	R	115	CTTCTTCTCCTGCTTCTGG	1mM
	Exon 1C	F	116	CGCCTCGTCCGTAC	1mM
30	Exon 1C	R	117	GTCGTCGTCGTCGTC	1mM
	Exon 1D	F	118	CCTCGGACGACGAC	3mM
	Exon 1D	R	119	GGATGATTCAGACGAGGA	3mM

Thermal cycling was performed with an initial denaturation step at 95°C  
for 10 min, followed by 35 cycles for exons 1A, 1B and 1C or 40 cycles for exon 1D  
35 of;

105

denaturation at 95°C for 30 sec, primer annealing at 55°C for 45 sec, and primer extension at 72°C for 2 min; followed by final extension at 72°C for 5 min.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the  
5 sequencing had the same sequence as the PCR primers except as shown in Table 11.

**Table 11. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Exon 1B	R	120	CAGCAGGCTCTGGTAGC
Exon 1C	F	121	GCGTGCGGGTAAGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 12.

15

**Table 12. Newly Identified ADRB1 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence	AA Change
Exon 1; 145 (AA 49)	122	CGCCAGCGAAAGCCCCGAGCC	
	123	CGCCAGCGAAGGCCCGAGCC	SER-GLY
20 Exon 1; 315	124	GCGCCGACCTGGTCATGGGGC	
	125	GCGCCGACCTGTTCATGGGGC	
Exon 1; 1165 (AA 389)	126	GGCCTTCCAGGGACTGCTCTG	
	127	GGCCTTCCAGCGACTGCTCTG	GLY-ARG
Exon 1; 1347	128	AGCCCTGGGCCGGCTGCAACG	
	25 129	AGCCCTGGGCGGGCTGCAACG	
3' UTR; +8	130	TAGGGCCCGGCGGGGCGCG	
	131	TAGGGCCCGGAGCGGGGCGCG	

SEQ ID NO:132 lists the sequence of the reference ADRB1 gene (GenBank Accession No. J03019), entire genomic sequence.

30

### Example 5

This example describes the identification of variants of the known aryl hydrocarbon receptor sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the aryl hydrocarbon receptor B1 (AHR) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 13. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 13.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
10 Exon 1	F	133	GTGCTCTGCTATTCAGC	1mM
Exon 1	R	134	CGCCAGTACAGGTGA	1mM
Exon 2	F	135	GGAAGATTTTAGAAAGACTTACG	2mM
Exon 2	R	136	GTAGTTATTAACACAGAAACAGC	2mM
Exon 3	F	137	CCACTGGCAACAGG	1mM
15 Exon 3	R	138	GGCAAAAAACATTGAGC	1mM
Exon 7	F	139	TGGAGAGAGGAGTGAAGG	1mM
Exon 7	R	140	GGAAGAATGTACGATAATAGC	1mM
Exon 10	F	141	GAGGTGAAAATAAAATATGTCC	1mM
Exon 10	R	142	TAATAAAAAATGCTGTCTCC	1mM

Thermal cycling was performed as described above in Example 3.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 14.

25

**Table 14.** Sequencing Primers

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Exon 1	F	143	CGCTCTGTTCGAGA
30 Exon 1	R	144	GAGGGGCGGAGACC
Exon 10	F	145	GAGGTGAAAATAAAATATGTCC
Exon 10	F	146	TACAGCATAATGAAAAACCT
Exon 10	R	147	TTATCTTGCCATTTCTGC
Exon 10	R	148	ATACACCTTGAGTTCAGAGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 15.

**Table 15. Newly Identified AHR Gene Polymorphisms**

Location	SEQ ID	Polymorphism Sequence	Change
5	NO		
5'UTR; +119	149	ACTGGTGGCCCGCGCCCGAGC	
	150	ACTGGTGGCCTGCGCCCGAGC	
5'UTR; +152	151	AAGCACCTGGATTTGGGAAG	
	152	AAGCACCTGAATTTGGGAAG	
10 5'UTR; +157	153	CCCTGGATTTGGGAAGTCCCG	
	154	CCCTGGATTAGGAAGTCCCG	
5'UTR; +240	155	CCACCGTGAGCGACCCAGGCC	
	156	CCACCGTGAGGGACCCAGGCC	
Exon 2; 132	157	ACCGACTTAATACAGAGTTGG	
15	158	ACCGACTTAACACAGAGTTGG	
Intron 3; +33	159	TCTTACACTAAGGACAGTTGTA	
	160	TCTTACACTAGACAGTTGTA	DEL AG
Exon 7; 771	161	AAGATGGATCAATACTTCCAC	
	162	AAGATGGATCTATACTTCCAC	
20 Intron 7; +33	163	TATTTTATTGGATGTACATTA	
	164	TATTTTATTGTATGTACATTA	
Exon 10; 1192	165	TTTACGAAAACGAAATACGAA	
	166	TTTACGAAAAAGAAATACGAA	
Exon 10; 1411 (AA 471)	167	TTATCTCTATCCTGCTTCAAG	
25	168	TTATCTCTATTCTGCTTCAAG	PRO-SER
Exon 10; 1664 (AA 554)	169	GAAGACATCAGACACATGCAG	
	170	GAAGACATCAAACACATGCAG	ARG-LYS
Exon 10; 1738 (AA 570)	171	TTCTGGTGAGGTTGACTTCAG	
	172	TTCTGGTGAGATTGACTTCAG	VAL-ILE
30	SEQ ID NO:173 lists the sequence of the reference AHR gene (GenBank Accession No. D31708), exon 1; SEQ ID NO:174 (GenBank Accession No. U27657), the 3' end of intron 1, all of exon 2 and the 5' end of intron 2; SEQ ID NO:175 (GenBank Accession No. U28060), the 3' end of intron 2, all of exon 3 and the 5' end of intron 3; SEQ ID NO:176 (GenBank Accession No. D38044), exon 7; and SEQ ID NO:177		
35	(GenBank Accession No. L19872-U28064-U28065), exon 10.		



**Example 6**

This example describes the identification of variants of the known aryl hydrocarbon receptor nuclear translocator sequence.

Using genomic DNA samples obtained from different individuals as the  
 5 initial template, PCR amplification of regions of the aryl hydrocarbon receptor nuclear translocator (ARNT) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 16. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

10 **Table 16.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 3	F	178	GCATCTGTTTAGTTCTATATCCT	1mM
Exon 3	R	179	CCCTCAACTCACCCACT	1mM
15 Exon 4	F	180	CTTCTTGTTCTCTGTCTGC	2mM
Exon 4	R	181	CTTCTCTACTTCTCATTGTCC	2mM
Exon 5	F	182	GTGACATAGAGAAAGTGAGG	1.5mM
Exon 5	R	183	TCTAATGCTGAGCCACA	1.5mM
Exon 8	F	184	CCTTCATTATTAGTAGCATTACC	1mM
20 Exon 8	R	185	AAGCCTGAGTTATCTATCTCC	1mM
Exon 10	F	186	AATGTGAAAGTTTAGAAAGTCC	2mM
Exon 10	R	187	CACCTGGTTTGACAAGC	2mM
Exon 17	F	188	AATAGGAAATAAGTGATGAGC	1mM
Exon 17	R	189	CTAAATAGATTGACACCTTGC	1mM
25 Exon 18	F	190	GAAAAGGCATTGATTGG	1mM
Exon 18	R	191	GCTTCAGGCTTCTAAGG	1mM
Exon 19	F	192	GCAAGCAGATTTTCTCC	1mM
Exon 19	R	193	ACAAACAGTGATTTTCTCC	1mM

Thermal cycling was performed as described above in Example 3 except  
 30 that the reactions using exon 4 or 5 primers were denatured for 40 cycles.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 17.

**Table 17. Sequencing Primers**

	Region	Forward/	SEQ ID	5'-3'
		Reverse	NO:	
5	Exon 3	F	194	CCTCCATTTCTCTCC
	Exon 4	F	195	CGGAACAAGATGACAGC
	Exon 4	R	196	TTAATGTTATAGCCAAGGACT
	Exon 5	F	197	GGTGTATGTGTCTGACTCC
	Exon 5	R	198	GCCAGAGTCAACAAACC
10	Exon 8	F	199	TTTTTTTTTTTCAAACCTCC
	Exon 8	R	200	AATAATGGAAGGGAAGG
	Exon 8	R	201	AAAGTAAGTGGGAGGTAAGG
	Exon 18	R	202	TGTTACTCACTAGAACTGAACG
	Exon 18	R	203	CCCAACCAAACACCTC

- 15 Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 18.

**Table 18. Newly Identified ARNT Gene Polymorphisms**

	Location	SEQ ID NO	Polymorphism Sequence	
20	Intron 3; +97	204	TCTTTGTATTTTCTTATCT	
		205	TCTTTGTATTCCTTATCT	
	Intron 4; +123	206	ACGAATTCAGTCCTTGGCTA	
		207	ACGAATTTCAATCCTTGGCTA	
	Exon 5; 667	208	TGGTGTATGTGTCTGACTCCG	
		209	TGGTGTATGTCTCTGACTCCG	
25	Intron 8; +18	210	AGTGAAATAGTAAATATTTC	
		211	AGTGAAATAGGAAATATTTC	
	Intron 10; +103	212	AACCTCAGTTGAGAAAAAGAG	
		213	AACCTCAGTTAAGAAAAAGAG	
30	Intron 16; -74	214	GACAGTGTGACTCTCATAGGCATGG	
		215	GACAGTGTGTCACCTAATAGGCATGG	
	Intron 17; -60	216	CTTGTGGCATATAGTACACAA	
		217	CTTGTGGCATTAGTACACAA	DEL A
35	3' UTR; +6	218	AATAGAACTATTGGGGTGAGG	
		219	AATAGAACTACTGGGGTGAGG	

SEQ ID NO:220 lists the sequence of the reference ARNT gene, exon 3; SEQ ID NO:221, exon 4; SEQ ID NO:222, exon 5; SEQ ID NO:223, exon 6; SEQ ID NO:224,

exon 7; SEQ ID NO:225, exon 8; SEQ ID NO:226, exon 9; SEQ ID NO:227, exon 10; SEQ ID NO:228, exon 13; SEQ ID NO:229, exon 14; SEQ ID NO:230 exon 15; SEQ ID NO:231, exon 16; SEQ ID NO:232, exon 17; SEQ ID NO:233, exon 18; and SEQ ID NO:234, exon 19.

5

#### Example 7

This example describes the identification of variants of the known cathepsin S sequence.

Using genomic DNA samples obtained from different individuals as the  
10 initial template, PCR amplification of regions of the cathepsin S (CTSS) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 19. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

15 **Table 19. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Promoter/Exon 1	F	235	TTTGAGTTTGATGAACGA	2mM
Promoter/Exon 1	R	236	ACAGAGTGTGAAGACCA	2mM
20 Exon 2	F	237	TCTCTATGAAAACAAGTGGT	2mM
Exon 2	R	238	GAGGTAGAAAACAGAACTCC	2mM
Exon 4	F	239	CACAATGAGAAAATCACCT	2mM
Exon 4	R	240	TCAGTGTCAAAATCTGTAGC	2mM
Exon 5	F	241	TTGTAAGACAGAAGGAAA	2mM
25 Exon 5	R	242	AGAACAGTCAGTCAGTGA	2mM

Thermal cycling was performed as described above in Example 3.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except for the  
30 promoter/Exon 1 primers as shown in Table 20.

**Table 20. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter/Exon 1	F	243	AATGGCTGAGTGAGAACC

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Promoter/Exon 1	F	244	TTTTTTTTGAGATAGGGTCT
Promoter/Exon 1	F	245	ACTTTGTCCCCAAGACC
Promoter/Exon 1	R	246	TTTTTATTAGGTGGGCATGG
Promoter/Exon 1	R	247	ACAGAGTGTGTTGAAGACCA

5 Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 21.

**Table 21.** Newly Identified CTSS Gene Polymorphisms

	Location	SEQ ID NO	Polymorphism Sequence	Change
10	Promoter; -521	248	AATGTTTTCCATGTAAAAGTT	
		249	AATGTTTTCCGTGTAAAAGTT	
	Promoter; -359	250	CATGCACCACCATGCCAGCT	
		251	CATGCACCACTATGCCAGCT	
	Promoter; -246	252	CAAGTGATCCTCCCGCCTGAGCCT	
15		253	CAAGTGATCCGCCTGAGCCT	DEL TCCC
	5' UTR; +41	254	GGACTCTTACTGTAGGAGCAA	
		255	GGACTCTTACCGTAGGAGCAA	
	5' UTR; +44	256	CTCTTACTGTAGGAGCAACTG	
		257	CTCTTACTGTGGGAGCAACTG	
20	Exon 2; 88 (AA 7)	258	CTGGTTTGTGTGCTCTTGGTG	
		259	CTGGTTTGTGCGCTCTTGGTG	VAL-ALA
	Exon 4; 405 (AA 113)	260	AAACCCTAATCGGATATTGCC	
		261	AAACCCTAATTGGATATTGCC	ARG-TRP
	Intron 4; -47	262	GAAGTCATTCCGAATGATTTT	
25		263	GAAGTCATTCTGAATGATTTT	

SEQ ID NO:264 lists the sequence of the reference CTSS gene (GenBank Accession No. U07369), exon 1; SEQ ID NO:265 (GenBank Accession No. U07370), exon 2; SEQ ID NO:266 (GenBank Accession No. U07371), exon 3; SEQ ID NO:267, exon 4; SEQ ID NO:268 (GenBank Accession No. U07372), exon 5; and SEQ ID NO:269  
 30 (GenBank Accession No. U07374), exon 6.

### Example 8

This example describes the identification of variants of the known cyclooxygenase 2 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the cyclooxygenase 2 (COX2) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 22. PCR amplification reactions were generally performed as described in

5 Example 1 using the following primers:

**Table 22.** PCR Primers and Mg<sup>++</sup> Concentration

	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
10	Promoter	F	270	TCACATTA ACTATTTACAGGGT	2mM
	Promoter	R	271	TATAAGACTGAAAACCAAGC	2mM
	Exon 3	F	272	TTATCCATTCTAAGGCAGG	2mM
	Exon 3	R	273	TATTTTGGCGATTAAGATG	2mM
	Exon 4	F	274	TTTTGGAGTTACATTCAACC	3mM
15	Exon 4	R	275	AAAAAATACCCATAGATAACC	3mM
	Exon 6 and 7	F	276	TTAGCAATTCATGGCTATG	3mM
	Exon 6 and 7	R	277	GCTATTTTATCAGTCATGCTTAC	3mM
	Exon 8	F	278	CTTTTGATACTGACAAGGAAG	3mM
	Exon 8	R	279	AACAAAGTTAGGCTTCTTATATC	3mM
20	Exon 9	F	280	GTTGAAATGTAGGTAAGCATC	1mM
	Exon 9	R	281	AGTGAGCCGAGATGG	1mM
	Exon 10A	F	282	GGATTACAGGCGTGAG	2mM
	Exon 10A	R	283	GATCATTAGACTTCTACAGTTCAG	2mM
	Exon 10B	F	284	CCACAGTACTACTAAAAGAACG	2mM
25	Exon 10B	R	285	CATGAAATTACTGGTAATGTC	2mM
	Exon 10C	F	286	GTCATCAAAACAAAACAGG	2mM
	Exon 10C	R	287	TCGTTATTCAAGCACAGC	2mM

Thermal cycling was performed as described above in Example 3 except that the reaction using exon 9 primers was amplified for 40 cycles.

30 The resulting PCR products were purified and sequenced using the methods described above in Example 1. The primers used for the sequencing had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 23.

35 **Table 23.** Sequencing Primers

113			
Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter	R	288	TTTATGTTTTAGTGACGACGC
Exon 3	F	289	CTATGGAGAAAAGTCTC
5 Exon 4	R	290	AATTTTTTTTTTTGGCAGCAATG
Exon 6 and 7	F	291	CAGGTATGCTTCCTTTGAC
Exon 6 and 7	R	292	GAGTATCTTTGACTGTGGG
Exon 10A	F	293	ACTGTTTTTTATTTTGTGAAGT
Exon 10A	F	294	CTTTGGTGGAGAAGTGGG
10 Exon 10A	R	295	TCATTAGACTTCTACAGTTCAGTC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 24.

**Table 24.** Newly Identified COX2 Gene Polymorphisms

15	Location	SEQ ID NO	Polymorphism Sequence	Change
	Promoter; -763	296	TACCTTCCCGCCTCTCTTC	
		297	TACCTTCCCCCCTCTCTTC	
	Promoter; -653	298	CTGAAGGTAGCTATTTTCATTC	
		299	CTGAAGGTAGTAGCTATTTTCATTC	INS TAG
20	Promoter; -605	300	TATGTATGTATGTGCTGCATA	
		301	TATGTATGTACGTGCTGCATA	
	Exon 3; 306	302	TGAGTTATGTCTTGACATGTA	
		303	TGAGTTATGTGTTGACATGTA	
	Exon 4; 437 (AA 146)	304	GATGATTGCCCGACTCCCTTG	
25		305	GATGATTGCCTGACTCCCTTG	PRO-LEU
	Intron 6; +38	306	AGTTATTACCGCTTATACCCA	
		307	AGTTATTACCACTTATACCCA	
	Intron 6; -25	308	TTAACTGATGTTTATTTATTATT	
		309	TTAACTGATGTTTATTATT	DEL TTTA
30	Exon 7; 732	310	AGATAATTGATGGAGAGATGT	
		311	AGATAATTGACGGAGAGATGT	
	Exon 7; 900	312	GAGTATGCGATGTGCTTAAAC	
		313	GAGTATGCGACGTGCTTAAAC	
	Intron 7; +111	314	AACTCACACATTCTATATACA	
35		315	AACTCACACACTCTATATACA	
	Exon 8; 1209	316	TGCTGGAACATGGAATTACCC	
		317	TGCTGGAACACGGAATTACCC	
	Intron 9; +72	318	GTTTCTTTTCGAGATGGAGC	

		114	
	319	GTTTTCTTTTGGAGATGGAGC	
Exon 10; 1532 (AA 511)	320	ATGGTAGAAGTTGGAGCACCA	
	321	ATGGTAGAAGCTGGAGCACCA	VAL-ALA
Exon 10; 1759 (AA 587)	322	TTCCCGCTCCGGA TAGATGA	
5	323	TTCCCGCTCCAGACTAGATGA	GLY-ARG
3' UTR; +277	324	TCAACTTATATTATAAGAACGAAAG	
	325	TCAACTTATAAGAACGAAAG	DEL TTATA
3' UTR; +427	326	TACTTTTGGTTATTTTCTGT	
	327	TACTTTTGGTCATTTTCTGT	
10	328	ATACCAAAAAGAAGCTGTCTT	
	329	ATACCAAAAACAAGCTGTCTT	
3' UTR; +678	330	TTTACTACAATTGCTTGTTA	
	331	TTTACTACAGTTGCTTGTTA	

SEQ ID NO:332 lists the sequence of the reference COX2 gene (GenBank  
 15 Accession No. U04636), entire genomic sequence.

#### Example 9

This example describes the identification of variants of the known  
 diazepam binding inhibitor sequence.

20 Using genomic DNA samples obtained from different individuals as the  
 initial template, PCR amplification of regions of the diazepam binding inhibitor  
 (DBI) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in  
 Table 25. PCR amplification reactions were generally performed as described in  
 Example 1 using the following primers:

25 **Table 25.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Promoter/Exon 1A	F	333	CTAAGCACCTACTTCCG	1mM
Promoter/Exon 1A	R	334	ATCAAGCACCTCGACTC	1mM
30 Exon 1B	F	335	ATGCCTAGCCCTGATTCTG	1mM
Exon 1B	R	336	GCACAGTATGCTGGAAAC	1mM
Exon 2	F	337	TTCAGGGGCTGCATTGC	1mM
Exon 2	R	338	CTGGAGACACTGAGAATC	1mM

Thermal cycling was performed as described above in Example 3. The  
 35 resulting PCR products were purified and sequenced using the methods

described above in Example 1. The primers used for the sequencing had the same sequence as the PCR primers.

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 26.

5

**Table 26. Newly Identified DBI Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
Promoter; -144	339	GCTACTCCCGGCGTTTGCGCA
	340	GCTACTCCCGACGTTTGCGCA
10 Intron 1A; -148	341	AGCACAGGGCAGGACGTCGCG
	342	AGCACAGGGCGGGACGTCGCG
Intron 1A; -106	343	TCCGTGGCCGGGAGCTTGGAG
	344	TCCGTGGCCGAGAGCTTGGAG
Intron 1A; -77	345	AAGTACGGGGCCGGCTGCTCA
	15 346	AAGTACGGGGTCGGCTGCTCA
Intron 1A; -53	347	TGCGGGACGAGGAGAATCGCG
	348	TGCGGGACGAAGAGAATCGCG
Intron 2; +29	349	GGAAGGGCATCTGCTCATCAA
	350	GGAAGGGCATATGCTCATCAA
20 Intron 2; +55	351	GCTCAGCAGCCCAGACTGGAA
	352	GCTCAGCAGCTCAGACTGGAA
Intron 2; +92	353	CTCTCAAACCTGCCTGAGGCC
	354	CTCTCAAACCTCCCTGAGGCC

SEQ ID NO:355 lists the sequence of exons 1 and 2 of the reference DBI gene  
25 (GenBank Accession No. X94563).

### Example 10

This example describes the identification of variants of the known epoxide hydroxylase 2 sequence.

30

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the epoxide hydroxylase 2 (EPHX2) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 27. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

35



**Table 27.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 1	F	356	ACCCGCCGCCATGAC	1mM
5 Exon 1	R	357	CCAGGTCTTCAGTTTCAT	1mM
Exon 2	F	358	AGTTCCTGGCAGTATCC	2mM
Exon 2	R	359	ATATTAGCAAGTATGTTTTAAGG	2mM
Exon 3	F	360	GGTCACAGGGAATGTATATG	2mM
Exon 3	R	361	TCTAATAGTGCTGCTTTTGC	2mM
10 Exon 4	F	362	AAGTGAGCACAACCTGC	2mM
Exon 4	R	363	GGGTAACAGTCTTCTAGGAG	2mM
Exon 5	F	364	GTTTTCATGCGTATGTTG	2mM
Exon 5	R	365	CAGTGGGTGATGGACTC	2mM
Exon 6	F	366	GAGGGAGATGGGCTG	1mM
15 Exon 6	R	367	GCTGGAGCACAGTGG	1mM
Exon 7	F	368	ATCCAGCAACGGACT	1mM
Exon 7	R	369	CTCCTGCCCCAACCT	1mM
Exon 8	F	370	CTGTGGCTCTTGGTTTG	2mM
Exon 8	R	371	ACAGGGCACCGTAGG	2mM
20 Exon 9	F	372	GATTTAGTAAGTTTTGTGGG	2mM
Exon 9	R	373	AGGAAGACCTGACACACAG	2mM
Exon 10	F	374	CATTTTACCTTAATCATCTCC	2mM
Exon 10	R	375	CAAAGGAATTCTCCAAAG	2mM
Exon 13	F	376	CATCTTGTATTTTATGCTAACC	2mM
25 Exon 13	R	377	TTTCCCAGTAGAGTGAGG	2mM
Exon 14	F	378	GCGTGGTACTCAGAGGTC	1mM
Exon 14	R	379	GTTAGAGTCAGCCCTATGC	1mM
Exon 15	F	380	TGGAGGCACTCATAAGG	1mM
Exon 15	R	381	AGCACCATAAAGTAGTGAGC	1mM
30 Exon 16	F	382	GACAGCAAGGCGTG	1mM
Exon 16	R	383	CATCCCAAGAGAAGCAC	1mM
Exon 17	F	384	ATCTCCAGTAATAACCACGAG	2mM
Exon 17	R	385	TGATGTTACTGATGATGTGC	2mM
Exon 18 and 19	F	386	TCATTCATTATTATCCC	2mM
35 Exon 18 and 19	R	387	CCCTCAGAACAAATGC	2mM

Thermal cycling was performed as described above in Example 3 except that the reaction using exon 6 primers was amplified for 40 cycles and the

annealing temperature for that sample was 58°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except the Exon 6 primer included a forward primer having the  
 5 sequence 5' CAGCCACCAGGAGGG 3' (SEQ ID NO:388) and the reverse primer having the sequence 5'CTTCCCAGGCTCAGG3' (SEQ ID NO:389), and the primers used to sequence exons 18 and 19 also included the forward primer having the sequence 5'CTGGTTTCATTGTGCTGGC 3' (SEQ ID NO:390) and the reverse primer having the sequence 5' AGCCATTCACACTTGTCTG 3' (SEQ ID  
 10 NO:391).

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 28.

**Table 28. Newly Identified EPHX2 Gene Polymorphisms**

15	Location	SEQ ID NO	Polymorphism Sequence	Change
	Intron 1; +68	392	CTGGGCTTG <b>C</b> AGCCCAGCTTT	
		393	CTGGGCTTG <b>C</b> GGCCCAGCTTT	
	Intron 1; -81	394	CTGCTTCTCAATGAATATGAA	
		395	CTGCTTCTCAGTGAATATGAA	
20	Exon 2; 164 (AA 55)	396	CGGCTTATGAAAGGAGAGATC	
		397	CGGCTTATGAGAGGAGAGATC	LYS- ARG
	Exon 3; 307 (AA 103)	398	AAAGATCAACCGCCCCATGCT	
		399	AAAGATCAACTGCCCCATGCT	ARG-
25	CYS			
	Intron 3; +31	400	AATCTCAGGCCGAACCA <b>C</b> CCA	
		401	AATCTCAGGCTGAACCA <b>C</b> CCA	
	Intron 3; +49	402	CCAGAACCCTCGGGAGCATT <b>A</b>	
		403	CCAGAACCCTTGGGAGCATT <b>A</b>	
30	Intron 3; +136	404	AAACATGGCCCCAAAGCAAGT	
		405	AAACATGGCCACA <b>A</b> AGCAAGT	
	Exon 4; 461 (AA 154)	406	ATAGAGTCGTGTCAGGTGGGA	
		407	ATAGAGTCGTATCAGGTGGGA	CYS- TYR
35	Exon 4; 489	408	AACCTGAACCTCAGATCTACA	
		409	AACCTGAACCA <b>C</b> AGATCTACA	

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Intron 4; +5	410	AGTGAGGTACGGAGACACTTC
	411	AGTGAGGTACAGAGACACTTC
Intron 4; +25	412	CCTTATGGCAGAGAAGGATGT
	413	CCTTATGGCACAGAAGGATGT
5 Exon 5; 591	414	GTGACTTGGGAATGGTCACCA
	415	GTGACTTGGGCATGGTCACCA
Intron 5; +21	416	TTCTGAGCGAGCCAAGCTTCC
	417	TTCTGAGCGAACCAAGCTTCC
Intron 5; -19	418	CTCTCTCACTATACCTTTCCT
	419	CTCTCTCACTGTACCTTTCCT
10 Exon 6; 687	420	CCCCCTGCGGACCTCTTGCA
	421	CCCCCTGCCAACCTCTTGCA
Intron 6; +25	422	TCTCTCAGTCGGCTAAGTGCT
	423	TCTCTCAGTCAGCTAAGTGCT
15 Intron 7; +69	424	GTGGTCCGACGTGGACTGTCG
	425	GTGGTCCGACATGGACTGTCG
Intron 7; -32	426	GACTGATGGGACCATGCTGGA
	427	GACTGATGGGTCCATGCTGGA
Exon 8; 860 (AA 287)	428	GCAGGTTACCGGGTCCTAGCT
20	429	GCAGGTTACCAGGTCCTAGCT
GLN		
Intron 8; +8	430	CCGGTGGGTGTGCTGTCTTGC
	431	CCGGTGGGTGCGCTGTCTTGC
Intron 8; -100	432	TTTGTGGGTTTTTGTGTTGTTG
25	433	TTTGTGGGTTGTTGTTGTTG
TTT		
Intron 8; -97	434	GTGGGTTTTTGTGTTGTTGTTT
	435	GTGGGTTTTTGTGTTGTTT
GTT		
30 Intron 9; -5	436	TGTCTTCTTCCTTAGGAGATG
	437	TGTCTTCTTCTTTAGGAGATG
Intron 12; -44	438	ACAGTTTCCACGATTTCTAGG
	439	ACAGTTTCCATGATTTCTAGG
Exon 13; 1209 (AA 403)	440	ACCTGAGTCGGACTTTCAAAA
35	441	ACCTGAGTCGTCGGACTTTCAAAA
INS		
ARG		
Exon 13; 1236	442	TCAGAGCAAGCGATGAGGTGA
	443	TCAGAGCAAGTGATGAGGTGA
Exon 13; 1237 (AA 413)	444	CAGAGCAAGCGATGAGGTGAG

		119	
	445	CAGAGCAAGCAATGAGGTGAG	ASP- ASN
Intron 13; +15	446	GGGGTGGGGATGGGTGCAGAA	
	447	GGGGTGGGGACGGGTGCAGAA	
5 Intron 13; -65	448	AGGGTTTTTCAGATGAGCATAT	
	449	AGGGTTTTTCATATGAGCATAT	
Intron 13; -60	450	TTTCAGATGAGCATATTCCT	
	451	TTTCAGATGAACATATTCCT	
Exon 14; 1275	452	TCTGTGAAGCGGGTAAGAGAC	
10	453	TCTGTGAAGCAGGTAAGAGAC	
Intron 15; +148	454	CCTCCAGTGTCGGGAGGCTCA	
	455	CCTCCAGTGTTGGGAGGCTCA	
Intron 16; +52	456	CCCGCCCGCGGGGCTTCCCAT	
	457	CCCGCCCGCGAGGCTTCCCAT	
15 Intron 16; +114	458	CAGATCTGCTGGCCACCTCCT	
	459	CAGATCTGCTAGCCACCTCCT	
Intron 16; -124	460	CGAGTCTGTTGTGCAAAGTTC	
	461	CGAGTCTGTTATGCAAAGTTC	
Intron 17; +35	462	GTCATCAGTGCACCCCGGGAG	
20	463	GTCATCAGTGTACCCCGGGAG	
Intron 17; -99	464	GGGTGGCCTGCGGGGAGCAGA	
	465	GGGTGGCCTGAGGGGAGCAGA	
Exon 19; 1593	466	CCCCCAGGCCAACCGAGGTGA	
	467	CCCCCAGGCCACCGAGGTGA	
25 3' UTR; +35	468	CAGGTGTGCCATCCTTCCACC	
	469	CAGGTGTGCCGTCCTTCCACC	
3' UTR; +93	470	ACACACATCTTGCATGGATGG	
	471	ACACACATCTCGCATGGATGG	

SEQ ID NO:472 lists the sequence of the reference EPHX2 gene (GenBank  
 30 Accession No. X97024), exon 1; SEQ ID NO:473 (GenBank Accession No. X97025),  
 exon 2; SEQ ID NO:474 (GenBank Accession No. X97026), exon 3; SEQ ID NO:475  
 (GenBank Accession No. X97027), exon 4; SEQ ID NO:476 (GenBank Accession  
 No. X97028), exon 5; SEQ ID NO:477 (GenBank Accession No. X97029), exon 6;  
 SEQ ID NO:478 (GenBank Accession No. X97030), exons 7 and 8; SEQ ID NO:479  
 35 (GenBank Accession No. X97031), exon 9; SEQ ID NO:480 (GenBank Accession  
 No. X97032), exon 10; SEQ ID NO:481 (GenBank Accession No. X97033), exon 11;  
 SEQ ID NO:482 (GenBank Accession No. X97034), exon 12; SEQ ID NO:483

(GenBank Accession No. X97035), exon 13; SEQ ID NO:484 (GenBank Accession No. X97036), exon 14; SEQ ID NO:485 (GenBank Accession No. X97037), exons 15 and 16; and SEQ ID NO:486 (GenBank Accession No. X97038), exons 17 through 19.

### 5 Example 11

This example describes the identification of variants of the known 5-lipoxygenase activating protein sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the 5-lipoxygenase activating protein (FLAP) gene were performed using the primers and MgCl<sub>2</sub> concentrations  
10 listed in Table 29. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 29. PCR Primers and Mg<sup>++</sup> Concentration**

15	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Promoter / Exon 1	F	487	CCACTGCCATTTATTCC	1.5mM
	Promoter / Exon 1	R	488	TAGGGTAAAAGTGTTGTGC	1.5mM
	Exon 2	F	489	GCTAAATGACAGTTGATGG	1mM
20	Exon 2	R	490	CACAAAGCCTCTCTGGT	1mM
	Exon 3	F	491	GGAAATACGAATGGGATT	2mM
	Exon 3	R	492	GCTCTCACCTCTCCAG	2mM
	Exon 5	F	493	AAGTAAATGGGAAAATGG	2mM
	Exon 5	R	494	AAAACCTCTCAACTATCAGC	2mM

25 Thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the same sequence as SEQ ID NOs:486, 490, or 493 and those shown in Table 30.

30 **Table 30. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter / Exon 1	F	495	TGCCACTCTGTCTGACC
Promoter / Exon 1	F	496	GCCACTGTGTAATTGTGC

			121	
	Promoter / Exon 1	R	497	TTTGAGGCTACAGTGAGC
	Promoter / Exon 1	R	498	ACTAACCACCAAAATGC
	Promoter / Exon 1	R	499	TTGTTTAAGCCTGACTTCC
	Exon 2	F	500	GGACATTTAGGGTTGCT
5	Exon 2	R	501	GTCCAACCTTCCTCACC
	Exon 3	F	502	GGAAATACGAATGGGATT
	Exon 3	R	503	AGGGCTTCACAGATGG
	Exon 5	F	504	GAGGGGAGATGGTGGT

- 10 Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 31.

**Table 31.** Newly Identified FLAP Gene Polymorphisms

	Location	SEQ ID NO	Polymorphism Sequence	Change
15	Promoter; -500	505	TGTGTGTGTGTGAGACAGTCTT	
		506	TGTGTGTGTGAGACAGTCTT	DEL TG
	Promoter; -263	507	TGCTGGGCTCGTGCTGGTCAT	
		508	TGCTGGGCTCATGCTGGTCAT	
	Promoter; -240	509	TCTTGGGTCCAGGATTCATTC	
20		510	TCTTGGGTCCCGGATTCATTC	
	5' UTR; +51	511	CAGAGCAGTCTTCTCTGGGGA	
		512	CAGAGCAGTCTTCTCTGGGGA	
	Intron 1; +18	513	AAGCCCTTCACTCAGGGAAGA	
		514	AAGCCCTTCAATCAGGGAAGA	
25	Intron 2; +12	515	TGAGTCCTAACCTGATGTTG	
		516	TGAGTCCTAACCTGATGTTG	
	Intron 2; +87	517	ATGTCTGTCTGAGCCAAGTTT	
		518	ATGTCTGTCTAAGCCAAGTTT	
	Intron 2; +95	519	CTGAGCCAAGTTTCTGAGCGC	
30		520	CTGAGCCAAGCTTCTGAGCGC	
	Intron 3; +64	521	GGTTCAAAGGGCAGGCTTTTT	
		522	GGTTCAAAGGTCAGGCTTTTT	
	3' UTR; +219	523	TGCTATTCCCATGCATTTTGT	
		524	TGCTATTCCCGTGCATTTTGT	

- 35 SEQ ID NO:525 lists the sequence of the reference FLAP gene (GenBank Accession No. M60470), exon 1; SEQ ID NO:526 (GenBank Accession No. M63259), exon 2;

SEQ ID NO:527 (GenBank Accession No. M63260), exon 3 and SEQ ID NO:528 (GenBank Accession No. M63261), exon 4.

### Example 12

5 This example describes the identification of variants of the known glutathione-S-transferase 12 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the glutathione-S-transferase 12 (GST12) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed  
10 in Table 32. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 32. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
15 Exon 2	F	529	TCCAAGATATTTTGAGAACA	3mM
Exon 2	R	530	ATCCATCTGTGCCAAAC	3mM
Exon 3	F	531	CTATGTTACCCAGGCTGA	2mM
Exon 3	R	532	AGAGGTCTCACTTTTTTCC	2mM
20 Exon 4	F	533	CCATTAGTGCTCAGATTAG	2mM
Exon 4	R	534	CCCCAGTTCATAATTCCTC	2mM

The thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing  
25 had the same sequence as the PCR primers.

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 33.

**Table 33. Newly Identified GST12 Gene Polymorphisms**

30 Location	SEQ ID NO	Polymorphism Sequence
Intron 1; -26	535	GTCTGCTTTTCCCATTAT
	536	GTCTGCTTTTCCCCATTAT
Intron 2; -84	537	CTGCCTCAGCCTCACAAAGCG
	538	CTGCCTCAGCGTCACAAAGCG

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Intron 3; -19	539	AGTGCTTTAATAGTTATCTTT
	540	AGTGCTTTAACAGTTATCTTT
3' UTR; +19	541	ATACAACTCAGCATCCAGTTG
	542	ATACAACTCAACATCCAGTTG
5 3' UTR; +57	543	TACTTCCAATTTATAATGAAT
	544	TACTTCCAATGTATAATGAAT

SEQ ID NO:545 lists the sequence of the reference GST12 gene (GenBank Accession No. U46495), exon 1 and 2; SEQ ID NO:546 (GenBank Accession No. U46497.1), exon 3; SEQ ID NO:547 (GenBank Accession No. U46498), exon 4.

10

### Example 13

This example describes the identification of variants of the known histamine-N-methyl transferase sequence.

Using genomic DNA samples obtained from different individuals as the  
 15 initial template, PCR amplification of regions of the histamine-N-methyl transferase (HNMT) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 34. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

20 **Table 34.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Promoter A	F	548	AAAAAAGAGAGTTGGGAAGT	1mM
Promoter A	R	549	GCACTCTCAGAAATCTACAGC	1mM
25 Promoter B	F	550	GGTTCCTCCTTCGTGA	2mM
Promoter B	R	551	CCAAAAAAAAAAAAAAAAATGCT	2mM
Exon 2	F	552	CCCATTTCCAAGTCTCC	2mM
Exon 2	R	553	GGTTGTCATCACACAGCA	2mM
Exon 3	F	554	GATGGCACTCACAGC	2mM
30 Exon 3	R	555	AACTGGGGAATGGAT	2mM
Exon 4	F	556	TGACTCTTTCTTTCACCTC	2mM
Exon 4	R	557	TCTTAGTATAATAAACATCTTTACC	2mM
3' UTR	F	558	ATTTTACTCTCTCCTCCTGT	2mM
3' UTR	R	559	AAGCACAATAGAAGAACG	2mM



The thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used included the PCR primers for Promoter A and exons 2, 3, 4, SEQ ID NO:551, and those shown in

5 Table 35.

**Table 35. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
10 Promoter B	F	560	TGAGTTACAACAAATCAGCA
Promoter B	F	561	TGGATTACAGCCTTGCT
Promoter B	R	562	ACTGTATTCAAATCACTTCCT
Promoter B	R	563	CCAAAAAAAAAAAAAAAAATGCT
3' UTR	F	564	AAAATGGAGACCTGCTTT
15 3' UTR	R	565	GCCAAATCAGTAACACAGG

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 36.

**Table 36. Newly Identified HNMT Gene Polymorphisms**

20 Location	SEQ ID NO	Polymorphism Sequence	Change
Promoter; -490	566	TGTCAGCGCGCTTAGGGAAG	
	567	TGTCAGCGCCCTTAGGGAAG	
Promoter; -458	568	CTGCACTTTTACCCTGGTGTC	
	569	CTGCACTTTTCCCTGGTGTC	DEL A
25 Promoter; -320	570	CTGAGTTACAACAAATCAGCA	
	571	CTGAGTTACAGCAAATCAGCA	
Promoter; -211	572	TGACAGTCTTTCGTTAAAGAT	
	573	TGACAGTCTTCCGTTAAAGAT	
Promoter; -159	574	TAGCTGTCCTCTTATCCTGG	
30	575	TAGCTGTCCTTTTATCCTGG	
Promoter; -125	576	GAACAGTCACTTTCCCACTTG	
	577	GAACAGTCACCTTCCCACTTG	
5' UTR; +108	578	AGCCTTTGTGGCATGTTAAAT	
	579	AGCCTTTGTGACATGTTAAAT	
35 Intron 1; -128	580	ATATAATTGGGACATTTTCATG	
	581	ATATAATTGGAACATTTTCATG	

		125		
Intron 3; +137	582	TGAATTAGTTCTTGGCAGGCA		
	583	TGAATTAGTTATTGGCAGGCA		
Exon 4; 314 (AA 105)	584	GTAGCCAAGACATCGAACCTC		
	585	GTAGCCAAGATATCGAACCTC	THR-ILE	
5 Intron 4; +48	586	GACTTTTCAGAAATATATATATA		
	587	GACTTTTCAGTATATATATA	DEL AA	
3' UTR; +60	588	TCACTCATTTGTTTCCATATT		
	589	TCACTCATTTATTTCCATATT		
3' UTR; +218	590	AGAGACCACATGCAGGCTCAA		
	591	AGAGACCACAAGCAGGCTCAA		

SEQ ID NO:592 lists the sequence of the reference HNMT gene (GenBank Accession No. U44106.1), exon 1; SEQ ID NO:593 (GenBank Accession No. U44107.1), exon 2; SEQ ID NO:594 (GenBank Accession No. U44108.1), exon 3; SEQ ID NO:595 (GenBank Accession No. U44109), exon 4; SEQ ID NO:596  
 15 (GenBank Accession No. U44110), exon 5; and SEQ ID NO:597 (GenBank Accession No. U44111), exon 6.

#### Example 14

This example describes the identification of variants of the known  
 20 kalleikrin 2 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the kalleikrin 2 (KLK2) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 37. PCR amplification reactions were generally performed as described in Example 1 using  
 25 the following primers:

**Table 37. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
30 Promoter / Exon 1	F	598	CTATCCTGGAGGCTGA	1mM
	R	599	GGAGAGAAAGGTCTGAGG	1mM
Exon 2	F	600	GGTCCAGCCACCAAC	1mM
Exon 2	R	601	CAGATACCAAGAGACACAGC	1mM
Exon 3	F	602	GTTTCTGTCTCTGCCTCT	1mM
35 Exon 3	R	603	CCACCTACACCATCTGG	1mM

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Exon 4	F	604	GCACAACCTGTTTGAGC	1mM
Exon 4	R	605	GGCGGCAGATGAGG	1mM
Exon 5	F	606	CCCTCTGTTGGACTCC	1mM
Exon 5	R	607	CCCTCCCATCTCTGC	1mM

- 5 The thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except as shown in Table 38.

10 **Table 38. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter / Exon 1	F	608	AGAATCGGTTGAGTCTGG
Promoter / Exon 1	F	609	CTCCCCCTCCACAGC
15 Promoter / Exon 1	R	610	CCTTCATTCTCCAGGAC
Promoter / Exon 1	R	611	AGTGTGGGCAAGAGGACT
Exon 2	F	612	GGTCCAGCCACCAAC
Exon 2	R	613	GGTCCAGCCACCAAC
Exon 5	F	614	GGGAGTGGGTCTGG
20 Exon 5	R	615	CGTCTTTGTGTGTCCT

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 39.

**Table 39. Newly Identified KLK2 Gene Polymorphisms**

25 Location	SEQ ID NO	Polymorphism Sequence	AA
Change			
Promoter; -214	616	TCACACCGTGGGAATGCCTCC	
	617	TCACACCGTGAGAATGCCTCC	
Intron 1; +62	618	AGCCCTTTTCCTCCCACCCAG	
30	619	AGCCCTTTTCGTCCCACCCAG	
Intron 1; +115	620	AGCCCAGACAATGTGCCCCTG	
	621	AGCCCAGACAGTGTGCCCCTG	
Intron 1; -4	622	CACCCCCTCCGCAGGTGCCGT	
	623	CACCCCCTCCACAGGTGCCGT	
35 Exon 3; 372	624	TCATGCTGCTCCGCCTGTCAG	
	625	TCATGCTGCTTCGCCTGTCAG	

		127	
Intron 3; +55	626	GTCTGAGGGAAGTGGGGCCA	
	627	GTCTGAGGGAGGTGGGGCCA	
Intron 3; -18	628	CACAGCCCAGTTTTTCTCTGA	
	629	CACAGCCCAGATTTTCTCTGA	
5 Intron 4; +100	630	GCCTCCCCTGCTCCCCAGCTA	
	631	GCCTCCCCTGATCCCCAGCTA	
Exon 5; 748 (AA 250)	632	GGTGCATTACCGGAAGTGGAT	
	633	GGTGCATTACTGGAAGTGGAT	ARG- TRP
10	SEQ ID NO:634 lists the sequence of the reference KLK2 gene (GenBank Accession No. M18157).		

### Example 15

This example describes the identification of variants of the known  
15 nicotinamide-N-methyl transferase sequence.

Using genomic DNA samples obtained from different individuals as the  
initial template, PCR amplification of regions of the nicotinamide-N-methyl  
transferase (NNMT) gene were performed using the primers and MgCl<sub>2</sub>  
concentrations listed in Table 40. PCR amplification reactions were generally  
20 performed as described in Example 1 using the following primers:

**Table 40. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
25 Promoter / Exon 1	F	635	AGACACTGGGTCATGG	1mM
Promoter / Exon 1	R	636	GCACTTTGTAAACTGTGGA	1mM
Exon 3	F	637	ACATCTGGGACAATACG	1mM
Exon 3	R	638	GGCAATGAAGACTGGAA	1mM

The thermal cycling was performed as described above in Example 3. The  
30 resulting PCR products were purified and sequenced using the methods  
described above in Example 1. The sequencing primers used are shown in Table  
41.

**Table 41. Sequencing Primers**

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Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter / Exon 1	F	639	TCCCTTCTTTTTTTCCT
Promoter / Exon 1	F	640	TTTCTCTGTTAGTGTTAACCA
5 Promoter / Exon 1	R	641	GGGATTGTAGACCAGAGG
Promoter / Exon 1	R	642	AAAGGGTGATGCCAAA
Exon 3	F	643	CAGACCTCCCCACCTAC
Exon 3	R	644	ATTGCTTGTA GACTGACCTC

Polymorphic sequences shown in bold were identified in the resulting  
 10 nucleotide sequences listed below in Table 42.

**Table 42.** Newly Identified NNMT Gene Polymorphisms

Location	SEQ ID NO	Polymorphism Sequence
Promoter; -292	645	GGTGCTTGTTAGGGGATGTCC
15	646	GGTGCTTGTTGGGGGATGTCC
Promoter; -228	647	TGACGAGCTCAAGTGCTCCCT
	648	TGACGAGCTCTAGTGCTCCCT
5' UTR; +86	649	GGGCAGTGCTCCAGTGGTACA
	650	GGGCAGTGCTTCAGTGGTACA
20 Intron 1; +44	651	GTGAGTCATATAGATGGAGTC
	652	GTGAGTCATACAGATGGAGTC
3' UTR; +71	653	TTGGGGCCCAATGGTTCATCT
	654	TTGGGGCCCAAGTGGTTCATCT

SEQ ID NO:655 lists the sequence of the reference NNMT gene (GenBank  
 25 Accession No. U20970), exon 1 and 2; and SEQ ID NO:656 (GenBank Accession  
 No. U20971), exon 3.

### Example 16

This example describes the identification of variants of the known NADPH  
 30 quinone oxidoreductase 2 sequence.

Using genomic DNA samples obtained from different individuals as the  
 initial template, PCR amplification of regions of the NADPH quinone  
 oxidoreductase 2 (NQO2) gene were performed using the primers and MgCl<sub>2</sub>  
 concentrations listed in Table 43. PCR amplification reactions were generally  
 35 performed as described in Example 1 using the following primers:

**Table 43. PCR Primers and Mg<sup>++</sup> Concentration**

	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
5	Exon 1	F	657	CCTCGGCGTGGTAGGCG	1mM
	Exon 1	R	658	GAAGTGTCTTCCCAAGTC	
	Exon 2	F	659	TTGACATCCTGCGTG	2mM
	Exon 2	R	660	AAAAAAAAGTCTTACTCCACA	
	Exon 3	F	661	CTTAGCTTCAATTACTATGATGC	2mM
10	Exon 3	R	662	ATCCCAGTGCTATCTATTTG	1mM
	Exon 4	F	663	TCTTTGACTTGTCTGAGGAG	
	Exon 4	R	664	GTAAGTGTGTCAACTGTGCTC	2mM
	Exon 5	F	665	CTGACCATAAGGGTTACC	
	Exon 5	R	666	TACATAGTGGGTGCTCAATC	
15	Exon 6	F	667	GTTGATTTGTCCATCCC	1.75mM
	Exon 6	R	668	GCTTCCATCCCATCTC	2mM
	Exon 7	F	669	AATCATTTAACCGAATGG	
	Exon 7	R	670	GATGGGATCAGAAGC	

Thermal cycling was performed as described above in Example 3 except that the exon 1 and 6 primers were amplified for 40 cycles and the annealing temperature of those samples was 58°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

The sequencing primers used for the sequencing had the same sequence as the PCR primers except as shown in Table 44.

**Table 44. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Exon 4	F	671	ATGGTTGGGATGGGCTGTG
30 Exon 4	R	672	GTAAGTGTGTCAACTGTGCTC
Exon 7	F	673	AATCATTTAACCGAATGG
Exon 7	R	674	CTCCTAGTGTGCTGCTTAC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 45.

**Table 45. Newly Identified NQO2 Gene Polymorphisms**

130		
Location	SEQ ID NO	Polymorphism Sequence
Promoter; -19	675	AGAGGCCTGCAGTCCCGCGGC
	676	AGAGGCCTGCGGTCCCGCGGC
5' UTR; +171	677	CCTACTGGGGCGTGCCTGGT
	678	CCTACTGGGGAGTGCCTGGT
Intron 1; +12	679	GAGTGATCCCCTGTCTGGGGAC
	680	GAGTGATCCCTTGTCTGGGGAC
Intron 1; +17	681	ATCCCCTGTCTGGGGACCGGGG
	682	ATCCCCTGTCTAGGGACCGGGG
Intron 1; -95	683	GATGTGTTTTCGTGTCTGTCA
	684	GATGTGTTTGTGTGTCTGTCA
Intron 1; -15	685	CCTCTGGGTTTGTCTTGTCTT
	686	CCTCTGGGTTTCGTTTGTCTT
Intron 2; +14	687	ATGATTCACTATTGTGGAGTA
	688	ATGATTCACTGTTGTGGAGTA
Exon 3; 93	689	ATGAACTGAGCAGGCAGGGCT
	690	ATGAACTGAGTAGGCAGGGCT
Exon 3; 47 (AA 16)	691	CAGGAACCCAAGTCTTTCAAC
	692	CAGGAACCCAGGTCTTTCAAC
Exon 3; 139 (AA 47)	693	TGCCATGAACTTTGAGCCGAG
	694	TGCCATGAACCTTGAGCCGAG
Intron 3; +36	695	TTATAAAAACCTATCTTTATGT
	696	TTATAAAAACCATCTTTATGT
Intron 3; +59	697	TTACTTTAAAAAATGTTGAC
	698	TTACTTTAAGAAATGTTGAC
Intron 3; -50	699	TGGTTGGGATGGGCTGTGGAT
	700	TGGTTGGGATGGCTGTGGAT
Exon 5; 330	701	TCAGCGTGCCGGCCATCCTGA
	702	TCAGCGTGCCAGCCATCCTGA
Exon 5; 405	703	TCTACGATTCCGGTTTGCTCC
	704	TCTACGATTCTGGTTTGCTCC
Intron 5; +21	705	TTGGATAAGGTTCACTATGGA
	706	TTGGATAAGGATCACTATGGA
Intron 5; -107	707	GAGGGTGTCCACACGCATGTT
	708	GAGGGTGTCCGCACGCATGTT
Exon 6; 438	709	CGCTCCTTTCCGTAACCACGG
	710	CGCTCCTTTCTGTAACCACGG
Intron 6; +84	711	ACACACACACACACACATA
	712	ACACACACACGCACACACATA

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Intron 6; +86	713	ACACACACACACACATACA
	714	ACACACACACGCACACATACA
Intron 6; +86	715	ACACACACACACACACATAC
	716	ACACACACACGCACACACATAC
5 Intron 6; +86	717	ACACACACACACACATACAT
	718	ACACACACACGCACACACATACAT
3' UTR; +38	719	CAGCACACTAGGAGGCCCAGG
	720	CAGCACACTACGAGGCCCAGG

SEQ ID NO:721 lists the sequence of the reference NQO2 gene, exon 1; SEQ ID  
 10 NO:722, introns 1 and 2 and exon 2; SEQ ID NO:723, introns 2 and 3 and exon 3;  
 SEQ ID NO:724, introns 3 and 4 and exon 4; SEQ ID NO:725, introns 4 and 5 and  
 exon 5; SEQ ID NO:726, introns 5 and 6 and exon 6; and SEQ ID NO:727, introns 5  
 and 6 and exon 6.

#### 15 Example 17

This example describes the identification of variants of the known  
 sulfotransferase thermolabile sequence.

Using genomic DNA samples obtained from different individuals as the  
 initial template, PCR amplification of regions of the sulfotransferase thermolabile  
 20 (STM) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in  
 Table 46. PCR amplification reactions were generally performed as described in  
 Example 1 using the following primers:

**Table 46. PCR Primers and Mg<sup>++</sup> Concentration**

25	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Exon 2	F	728	GCAGAGGAGTTTCTTCAGG	2mM
	Exon 2	R	729	CTCCCCTCAGCATCC	2mM
	Exon 4	F	730	CCAAAAAAGAGAGAATCC	3mM
30	Exon 4	R	731	CTATTTCATAAACAGTCCTC	3mM
	Exon 10	F	732	GATCTATTCAATTTACTCCAGA	2mM
	Exon 10	R	733	TACTTCTCCAAACCCTTC	2mM

Thermal cycling was performed as described above in Example 3 except  
 that the reaction using exon 4 primers was amplified for 40 cycles, the primers for



exons 2 and 4 were annealed at 55°C, and the exon 10 primers were annealed at 60°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the same sequence as the PCR primers except, or with the addition of, the primers  
5 shown in Table 47.

**Table 47. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
10 Exon 2	R	734	GCACAGAAAAGAGGTAGGAG
Exon 4	R	735	GCCCTCCTCACTTACCA
Exon 10	F	736	CGTCCCCCAGGAGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 48.

15

**Table 48. Newly Identified STM Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence	AA Change
Intron 1; -70	737	ATCTCAGCATGCAGGGCGGAT	
	738	ATCTCAGCATCCAGGGCGGAT	
20 Intron 1; -64	739	GCATGCAGGGCGGATACTGGA	
	740	GCATGCAGGGTGGATACTGGA	
Exon 4; 105	741	AGAGCTTCCAAGCCCCGACCTG	
	742	AGAGCTTCCAGGCCCGACCTG	
3' UTR; +367	743	AATAAAGCTCAATTAAAATAAAAT	
	25 744	AATAAAGCTCAAAAATAAAAT	DEL AATT

SEQ ID NO:745 lists the sequence of the reference STM gene (GenBank Accession No. U20499).

**Example 18**

30 This example describes the identification of variants of the known UDP-glucuronosyl transferase 2B4 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the UDP-glucuronosyl transferase 2B4 (UGT2B4) gene was performed using the primers and MgCl<sub>2</sub> concentrations

listed in Table 49. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 49. PCR Primers and Mg<sup>++</sup> Concentration**

5	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Promoter 1A	F	746	TCGTGGAGAGTCTTGC	1mM
	Promoter 1A	R	747	TGAGGTATTCCTTCAGGTC	1mM
	Promoter 1B	F	748	CTTGTGGGGTCCTTG	1mM
10	Promoter 1B	R	749	CATAAGAGTAGCAGTGAGAGG	1mM
	Promoter 1C	F	750	TTTTTGAACCACATTTAGC	2mM
	Promoter 1C	R	751	GATTTTTTTTTTTTGAGAGC	2mM
	Promoter 1D	F	752	AAGGTCAGGGGTTTCG	1mM
	Promoter 1D	R	753	CTGTATCAGCAGAAGAGC	1mM

15 Thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used included SEQ ID NO:746, 748, 750, 751 or 753 and those shown in Table 50.

20 **Table 50. Sequencing Primers**

	Region	Forward/ Reverse	SEQ ID NO:	5'-3'
	Promoter 1A	F	754	TCTATTGTTGTCATTTTCAGC
	Promoter 1A	F	755	CAATGAGACATTATGTTTTGC
25	Promoter 1A	R	756	ATGAGGAGTTACTTCTTATGG
	Promoter 1A	R	757	CCTCCAACATCTTCCTTC
	Promoter 1A	R	758	CCTTCAGGTCCAGCAT
	Promoter 1B	F	759	CCTCCCTTTGTCCTTC
	Promoter 1B	F	760	AGTTGCCCAGGATAGGAC
30	Promoter 1B	R	761	AAAGTAAACCAAGCCTGT
	Promoter 1B	R	762	GCAATTTGTCCTATCCTG
	Promoter 1B	R	763	GAGAGGCTCATGTTCTG
	Promoter 1D	F	764	AAGAAGAACATTAAACGCACT

Polymorphic sequences shown in bold were identified in the resulting  
35 nucleotide sequences listed below in Table 51.

**Table 51.** Newly Identified UGT2B4 Gene Polymorphisms

	Location	SEQ ID NO	Polymorphism Sequence
5	Promoter; -1818	765	TTTCAGCAATGTTACATAAT
		766	TTTCAGCAATATTCACATAAT
	Promoter; -1746	767	TAAGAAGTAACTCCTCATGTA
		768	TAAGAAGTAATTCCTCATGTA
	Promoter; -1373	769	ATCAGTAGGAGTTGGAACTG
10		770	ATCAGTAGGAATTGGAACTG
	Promoter; -1217	771	CAAAATGTTTAAGTTATTATC
		772	CAAAATGTTTCAGTTATTATC
	Promoter; -1125	773	TATTAGGAAGCGAGTCAGAGA
		774	TATTAGGAAGTGAGTCAGAGA
15	Promoter; -1053	775	TTTTTTTTTTCCCCTCCCTTT
		776	TTTTTTTTTTCCCCTCCCTTT
	Promoter; -946	777	CGTAAATGCTATATCATAAAT
		778	CGTAAATGCTGTATCATAAAT
	Promoter; -827	779	CTATAGAGACAGAAATTCAAG
20		780	CTATAGAGACTGAAATTCAAG
	Promoter; -747	781	AGCTTATAGGCTTTATTTTTA
		782	AGCTTATAGGTTTATTTTTA
	Promoter; -507	783	GCACACTATTCTGAAATATAT
		784	GCACACTATTTTGAAATATAT
25	Promoter; -180	785	TCAAAAAAAAAAAAAATCCAAA
		786	TCAAAAAAAAAATAAATCCAAA
	Promoter; -125	787	CTACCTTTTAGTTGTCTCTTT
		788	CTACCTTTTATTTGTCTCTTT

SEQ ID NO:789 lists the sequence of the reference UGT2B4 gene.

### 30 Example 19

This example describes the identification of variants of the known UDP-glucuronosyl transferase 2B7 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the UDP-glucuronosyl transferase  
 35 2B7 (UGT2B7) gene was performed using the primers and MgCl<sub>2</sub> concentrations

listed in Table 52. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 52. PCR Primers and Mg<sup>++</sup> Concentration**

5	Region	Forward/	SEQ ID	5'-3'	[Mg <sup>++</sup> ]
		Reverse	NO		
	Promoter 1A	F	790	AGCTGGCATCAGTGAAGTCT	1mM
	Promoter 1A	R	791	CCTGTCCTAGGTAATTGCTA	1mM
	Promoter 1B	F	792	GAATCAACATGTATACGCTA	1mM
10	Promoter 1B	R	793	GATCTTGTTTCTGCAGTCCA	1mM
	Promoter 1C	F	794	CTGATTGTTATGGTAGATGC	1mM
	Promoter 1C	R	795	CACCTTCCACAATTCCCAG	1mM

Thermal cycling was performed as described above in Example 3. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used are shown in Table 53.

**Table 53. Sequencing Primers**

20	Region	Forward/	SEQ ID	5'-3'
		Reverse	NO:	
	Promoter 1A	F	796	CTGGCATCAGTGAAGTCT
	Promoter 1A	F	797	GCTGAATGTACTACAAGC
	Promoter 1A	R	798	CTAGGTAATTGCTAATTG
	Promoter 1A	R	799	ACAACCATCATGTAAGAT
25	Promoter 1B	F	800	ACATGTATACGCTATATC
	Promoter 1B	F	801	CTAAGGACTATAGGGCTT
	Promoter 1B	R	802	AATCAGTTGGAGAGCCCT
	Promoter 1B	R	803	GCAGTCCATTTGACACAA
	Promoter 1C	F	804	CTGAAGGATAGCACTCAT
30	Promoter 1C	F	805	ATGGTAGATGCACAATTC
	Promoter 1C	R	806	AACAGTCTGAGCATGTGG
	Promoter 1C	R	807	TTCCACAATTCCCAGAGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 54.

**Table 54. Newly Identified UGT2B7 Gene Polymorphisms**

	Location	SEQ ID NO	Polymorphism Sequence
5	Promoter; -1099	808	CAGTGAAGTCTTTCAGATCAT
		809	CAGTGAAGTCCTTCAGATCAT
	Promoter; -886	810	GAAGTGAGTCGGAGAACAAGC
		811	GAAGTGAGTCAGAGAACAAGC
	Promoter; -721	812	AACATGTATACGCTATATCAT
		813	AACATGTATATGCTATATCAT
10	Promoter; -520	814	GGACTATAGGGCTTATTTTGG
		815	GGACTATAGGACTTATTTTGG
	Promoter; -313	816	TGCAGAAACAAGATCTGTCAC
		817	TGCAGAAACAGGATCTGTCAC
	Promoter; -147	818	CATTTGTCTCTTTGCCATCCA
15		819	CATTTGTCTCCTTGCCATCCA
	Promoter; -124	820	TGCTCAGACTGTTGATTTAAT
		821	TGCTCAGACTATTGATTTAAT
	Promoter; -111	822	GATTTAATGATATTGTATGTA
		823	GATTTAATGACATTGTATGTA
20	Promoter; -18	824	AAAGGAACAGCAACTGGAAAA
		825	AAAGGAACAGTAACTGGAAAA

SEQ ID NO:826 lists the sequence of the reference UGT2B7 gene.

### Example 20

25 This example describes the identification of variants of the known UDP-glucuronosyl transferase 2B15 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the UDP-glucuronosyl transferase 2B15 (UGT2B15) gene was performed using the primers and MgCl<sub>2</sub> 30 concentrations listed in Table 55. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 55. PCR Primers and Mg<sup>++</sup> Concentration**

	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
35	Promoter 1A	F	827	AACATGCTGTTTAAATGAACG	1mM

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Promoter 1A	R	828	CCCCAAGATACAAGACCA	1mM
Promoter 1B	F	829	GCCTATTTCTTGATCTTCAGG	2mM
Promoter 1B	R	830	AACTGCCAGAACAGACCAG	2mM
Promoter 1C	F	831	GATCCTCTCAGAATTGCT	2mM
5 Promoter 1C	R	832	GCTATGCTTCTTTCCAGT	2mM

- Thermal cycling was performed as described above in Example 3 except the primer annealing was performed at 60°C and the sample using promoter 1A primers was amplified for 40 cycles annealed at 62°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1.
- 10 The sequencing primers used had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 56.

**Table 56. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
15 Promoter 1B	F	833	CCAGGCAGGAATGAGC
Promoter 1B	R	834	AGCCAAGCAAAATACAGG
Promoter 1C	F	835	CTAGGGTAGGATGGATGC
Promoter 1C	F	836	GCCTCTCACTTGCCACT
20 Promoter 1C	R	837	CCCACTCTGAACTTTTGC
Promoter 1C	R	838	GACCTAGAATATGTAAGTAACCTGT

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 57.

**Table 57. Newly Identified UGT2B15 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
Promoter; -1399	839	GGCCTAAAATGGCATCAGCCCC
	840	GGCCTAAAATAGCATCAGCCCC
Promoter; -1387	841	CATCAGCCCCCAGTGAGGATG
30	842	CATCAGCCCCAAGTGAGGATG
Promoter; -1129	843	AGCCTTCAGGCCCTGAGGAGA
	844	AGCCTTCAGGTCCTGAGGAGA
Promoter; -932	845	CTTCTCCTGCAAACAGAACTT
	846	CTTCTCCTGCCAACAGAACTT
35 Promoter; -852	847	TGTTGGGGCACTCACAGTGTT
	848	TGTTGGGGCAGTCACAGTGTT

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Promoter; -808	849	GGAGCAGTACGCTTCCTGCAG
	850	GGAGCAGTACTCTTCCTGCAG
Promoter; -503	851	CTGATTATTGTAGTGAAAGTA
	852	CTGATTATTGCAGTGAAAGTA
5 Promoter; -498	853	TATTGTAGTGAAAGTAAAATT
	854	TATTGTAGTGGAAGTAAAATT
Promoter; -496	855	TTGTAGTGAAAGTAAAATTCT
	856	TTGTAGTGAATGTAAAATTCT
Promoter; -487	857	AAGTAAAATTCTGTGAATATA
10 Promoter; -432	858	AAGTAAAATTTTGTGAATATA
	859	AGTCATATGGTATATGAATTA
	860	AGTCATATGGCATATGAATTA
Promoter; -383	861	CTTGCAACCACGATATTAATA
	862	CTTGCAACCACAATATTAATA
15 Promoter; -368	863	TAAAAAATGCCGTTTGAGTTG
	864	TAAAAAATGCTGTTTGAGTTG
Promoter; -207	865	TAGAGTAATTGTAAACATAAA
	866	TAGAGTAATTATAAACATAAA

SEQ ID NO:867 lists the sequence of the reference UGT2B15 gene .

20

### Example 21

This example describes the identification of variants of the known urokinase sequence.

Using genomic DNA samples obtained from different individuals as the  
 25 initial template, PCR amplification of regions of the urokinase (uPA) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 58. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

30 **Table 58. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 2	F	868	ATAGAGGAGAGAGACAGC	1mM
Exon 2	R	869	AAGACCATGGTTCCAGC	1mM
35 Exon 3	F	870	AGGGAAGAGTGGGTTTTG	2mM
Exon 3	R	871	TACCTCCAGCTCCTAACT	2mM

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Exon 6	F	872	TGGTTGAGTCTTCCCTGA	1mM
Exon 6	R	873	GGAAGGAGAAAGGGATGT	1mM
Exon 8	F	874	ACAAGTCGTGCTTTGAGG	2mM
Exon 8	R	875	TATCGAGGCTTCAAGGTC	2mM
5 Exon 9 and 10	F	876	GGGATAGGCATAGCTACT	2mM
Exon 9 and 10	R	877	TCTGGGGAGATATGGAAG	2mM
Exon 11A	F	878	ATGGGAAGTCGCTAAGGA	2mM
Exon 11A	R	879	AGTCGTTAGTGTCTCTGC	2mM
Exon 11B	F	880	AGCTTAGCCAATGTGGGA	2mM
10 Exon 11B	R	881	ACTCCAACCTCCTCCCAT	2mM

Thermal cycling was performed as described in Example 3 except at an annealing temperature of 56°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers  
 15 except as shown in Table 59.

**Table 59. Sequencing Primers**

Region		Forward/ Reverse	SEQ ID NO:	5'-3'
20	Exon 2	R	882	TGCCACCCTGTCCCATTTC
	Exon 3	R	883	CCTCCATTTAGACAGTCTC
	Exon 6	R	884	ATTCTTCTGGAGGAGAGG
	Exon 8	F	885	GGCATGATTTCATGGGAC
	Exon 8	R	886	TTATGGCCACAGTAGTCG
25	Exon 9 and 10	F	887	TGCGACTGACTTAGAAGG
	Exon 9 and 10	R	888	TTACCTTTGCAGCCCATC
	Exon 9 and 10	R	889	TCTGGGGAGATATGGAAG
	Exon 11A	F	890	AGAGTCATCTCCATCAGC
	Exon 11A	R	891	AGTCGTTAGTGTCTCTGC
30	Exon 11B	F	892	CTGGAGAGGTTATAGGTC
	Exon 11B	R	893	ACTCCAACCTCCTCCCAT

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 60.

35 **Table 60. Newly Identified uPA Gene Polymorphisms**



		140	
Location	SEQ ID NO	Polymorphism Sequence	AA
Change			
5' UTR; +22	894	CGCCGTCTAGCGCCCCGACCT	
	895	CGCCGTCTAGAGCCCCGACCT	
5 Intron 2; +28	896	TTGACTGATGCTGCCCAAGGA	
	897	TTGACTGATGATGCCCAAGGA	
Intron 3; +49	898	AGTTGGGAAGGCTTCAGGGGA	
	899	AGTTGGGAAGACTTCAGGGGA	
Exon 6; 422 (AA 141)	900	GGCCTAAAGCCGCTTGTCCAA	
10	901	GGCCTAAAGCTGCTTGTCCAA	PRO-
LEU			
Intron 7; -7	902	GGTATCTTCTTCCACAGTGAT	
	903	GGTATCTTCTCCCACAGTGAT	
Exon 8; 691 (AA 231)	904	TGATTACCCAAAGAAGGAGGA	
15	905	TGATTACCCACAGAAGGAGGA	LYS-
			GLN
Exon 8; 822	906	CTCACCACAACGACATTGGTG	
	907	CTCACCACAATGACATTGGTG	
Intron 9; +66	908	ATGAGCCCAGTGTGATCAAGG	
20	909	ATGAGCCCAGCGTGATCAAGG	
Intron 9; -125	910	TCAGATTTGCATGGAGAGAGA	
	911	TCAGATTTGCGTGGAGAGAGA	
3' UTR; +141	912	CCCACCAGGGTGAACGACAAT	
	913	CCCACCAGGGCGAACGACAAT	
25 3' UTR; +753	914	CTCAGTTTCACTTTCACATAG	
	915	CTCAGTTTCATTTTCACATAG	
3' UTR; +844	916	ACCACTCCTGGTACACTGAAT	
	917	ACCACTCCTGTACACTGAAT	DEL G

SEQ ID NO:918 lists the sequence of the reference uPA gene (GenBank Accession  
 30 No. X02419), entire genomic sequence.

### Example 22

This example describes the identification of variants of the known multidrug resistance gene 1 sequence.

35 Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the multidrug resistance gene 1 (MDR1) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed

in Table 61. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 61. PCR Primers and Mg<sup>++</sup> Concentration**

5	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Promoter A.1	F	919	CACAAAAGCAAGACTGGT	2mM
	Promoter A.1	R	920	GGATTAGGCTTCTAACAGG	2mM
	Promoter A.2	F	921	CTCACGCCTGTAATCC	1mM
10	Promoter A.2	R	922	TCTATGACTTTCACATATTACC	1mM
	Promoter B Exon 1	F	923	TTTTTTTACTGAGATGAAACC	2mM
	Promoter B Exon 1	R	924	CGTCCTACACCTTAGCAA	2mM
	Exon 2	F	925	CCAACAACTTCTGCTCT	1mM
	Exon 2	R	926	GCTCCCTCTTACTGCTCT	1mM
15	Exon 3	F	927	GCATTCTCCTGAAAATAAGC	2mM
	Exon 3	R	928	GGGGTCATACTATTATCATCC	2mM
	Exon 5	F	929	AAACTATCAAGAGTATTGTTCTCC	2mM
	Exon 5	R	930	GAATGAATGCCATAATGC	2mM
	Exon 6	F	931	GGGAACAAAAGGATGC	1mM
20	Exon 6	R	932	CCAGATAAGTGAAAAAATAGGAA	1mM
	Exon 7	F	933	GAACAGAATGGAGTCTTGG	1mM
	Exon 7	R	934	GCTAAATAAAACAAAGCATAGG	1mM
	Exon 9	F	935	GGGATTACAGGTGTGAGC	1mM
	Exon 9	R	936	ATAGGGTCAATGTATGAGCA	1mM
25	Exon 10 & 11	F	937	AGTGAGAAAAAAACATCAAGG	1mM
	Exon 10 & 11	R	938	AAGTATGAAAAAAAATGCTGT	1mM
	Exon 12 & 13	F	939	TTCCCTTCTTCCGATT	2mM
	Exon 12 & 13	R	940	CAGTCAGTTCCTATATCCTGT	2mM
	Exon 14	F	941	CAAAGAGACCCAATGCT	1.75mM
30	Exon 14	R	942	GGCTGTGTATAGGTTTCCT	1.75mM
	Exon 15	F	943	AAACACTGGTCTCATCCTG	1mM
	Exon 15	R	944	ATTTATTGAAGTCAGAGGCTAT	1mM
	Exon 16	F	945	GGGATAGGACAGGAGGAT	1mM
	Exon 16	R	946	AAACAACACAGCAGATTAGC	1mM
35	Exon 17	F	947	TGTGATGACTAAGGAAGGTTT	1mM
	Exon 17	R	948	AAATAAAAGTAAGTGTGTTGTGGA	1mM
	Exon 19	F	949	AGTAGAGCCTCATCTGTGC	1mM

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	Exon 19	R	950	CCGTA <del>CTGCCTTGTGC</del> 1mM
	Exon 21	F	951	TTAGAGCATAGTAAGCAGTAGG 2mM
	Exon 21	R	952	ATAGCAAATCTTGGGACA 2mM
	Exon 25	F	953	GGCTCTCAGACTTTATCCA 1mM
5	Exon 25	R	954	AGCAGTTTGAAGTGAAGC 1mM
	Exon 28A	F	955	CCCACAAAAATGAGTAGG 1mM
	Exon 28A	R	956	TGCTCACCGCCTGT 1mM
	Exon 28B	F	957	AGGCAGTCAGTTACAGTCC 1mM
	Exon 28B	R	958	GCACCCACCACCAA 1mM
10	Thermal cycling was performed as described in Example 3 except fragment A.2 of the promoter and fragment B of exon 28 were amplified over 40 cycles at an annealing temperature of 60°C. Also, exon 9 was amplified for 40 cycles. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the same			
15	sequence as the PCR primers except, or with the addition of, the primers shown in Table 62.			

**Table 62. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
20			
Promoter A.1	F	959	ACTGGTGTCTATCAAGAAACC
Promoter A.1	R	960	GCCACTATTTTTTCCACA
Promoter A.2	F	961	GCGGATCAÇGAGGTC
Promoter A.2	R	962	TCTATGACTTTCACATATTACC
25	Promoter B & Exon 1 R	963	CTCCTCCTCTGGTACTGG
Exon 6	F	964	GGATTTTGTCTCATAAGTACCTT
Exon 7	F	965	GCAGGAAGGGAGAAGG
Exon 9	F	966	CTGAGAGGACCAAGGTG
Exon 9	F	967	GCCTTCCACTTTTAACTAG
30	Exon 9	968	CACAGGACTGAACACATCC
Exon 10 & 11	F	969	GCTGTCAATACTTGGCTTC
Exon 10 & 11	R	970	TTTCTTTGTCACTTTATCCAG
Exon 12 & 13	F	971	ACCACACCAATGATTTC
Exon 12 & 13	R	972	TTTCTGATGTTGCCCTTT
35	Exon 14	973	GAAGGAATCACCTAGAAGC
Exon 14	R	974	TAAAATATGAGCAGAGATAGC
Exon 17	F	975	AATGGCACAAAATACACC

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Exon 17	R	976	TTTTGGAGGATTATGAAGC
Exon 28A	F	977	AGGCAGTCAGTTACAGTCC
Exon 28A	F	978	TCATTATTCTGTAAGTGTTTGCT
Exon 28A	R	979	AGGTATCTGTTTAACATTTTCCTC
5 Exon 28B	F	980	AATAGATGCCTTTCTGTGC

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 63.

**Table 63. Newly Identified MDR1 Gene Polymorphisms**

	Location	SEQ ID NO	Polymorphism Sequence	Change
10	Promoter 1; -479	981	CATAGTCATGTACTCAAAATT	
		982	CATAGTCATGCACTCAAAATT	
	Promoter 1; -299	983	CTGTGAAGAGTAGAACATGAA	
		984	CTGTGAAGAGCAGAACATGAA	
15	Promoter 2; -1653	985	TGAAAGGTGAGATAAAGCAAC	
		986	TGAAAGGTGAAATAAAGCAAC	
	Promoter 2; -1350	987	CGAGGCGGGCGGATCACGAGG	
		988	CGAGGCGGGCAGATCACGAGG	
	Promoter 2; -1210	989	AGGAGAATGGTGTGAACCCGG	
20		990	AGGAGAATGGCGTGAACCCGG	
	5' UTR; +140	991	TTCAGGTCGGAATGGATCTTG	
		992	TTCAGGTCGGGATGGATCTTG	
	Exon 2; 61 (AA 21)	993	TAAACTGAACAATAAAAGGTA	
		994	TAAACTGAACGATAAAAGGTA	ASN-ASP
25	Intron 3; +36	995	CAAAATACTTCGGAAATTTGA	
		996	CAAAATACTTTGGAAATTTGA	
	Intron 4; -25	997	GACATAAATGGTATGTTTGTT	
		998	GACATAAATTGTATGTTTGTT	
	Intron 5; +66	999	AAACTTTGCATTATCATCACA	
30		1000	AAACTTTGCAGTATCATCACA	
	Intron 6; +139	1001	TAAGCAGCAATAATGTCGTGT	
		1002	TAAGCAGCAACAATGTCGTGT	
	Exon 8; 781 (AA 261)	1003	CTTGGCAGCAATTAGAACTGT	
		1004	CTTGGCAGCAGTTAGAACTGT	ILE-VAL
35	Intron 8; -106	1005	GACAAAATGCATGTATATCAC	
		1006	GACAAAATGCGTGTATATCAC	
	Intron 10; -41	1007	TAAAAGTAGTTATTGTAACCT	
		1008	TAAAAGTAGTGATTGTAACCT	

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Exon 12; 1236	1009	TCTTGAAGGGTCTGAACCTGA	
	1010	TCTTGAAGGGCCTGAACCTGA	
Intron 12; +44	1011	GATCAGCAGT CACATTGCACA	
	1012	GATCAGCAGTTACATTGCACA	
5 Intron 13; +24	1013	GCCCTTTGCCCTTCTAGAGGT	
	1014	GCCCTTTGCCCTTCTAGAGGT	
Intron 13; +81	1015	TAGGAAACTACTATAAAATCGG	
	1016	TAGGAAACTATTATAAAATCGG	
10 Intron 14; +38	1017	TGATTTATAAGCATAAGAACA	
	1018	TGATTTATAAACATAAGAACA	
Intron 15; +38	1019	AGTCATCTCAGTGATAAACTG	
	1020	AGTCATCTCAATGATAAACTG	
Intron 16; +73	1021	CTAGGGCTACAGTAGGAGTGG	
	1022	CTAGGGCTACGGTAGGAGTGG	
15 Intron 16; -76	1023	ATTCCTTTACTAATTTTGTG	
	1024	ATTCCTTTACAAATTTTGTG	
Intron 18; -88	1025	GACTTTGTCTGATCTCCTGCT	
	1026	GACTTTGTCTAATCTCCTGCT	
20 Intron 18; -35	1027	TTAAATGGTGGCTGGGTCCCT	
	1028	TTAAATGGTGCCTGGGTCCCT	
Intron 19; +129	1029	TCAGTCTCACGTCAGAGATGC	
	1030	TCAGTCTCACATCAGAGATGC	
Exon 21; 2650	1031	TGGACAAGCACTGAAAGATAA	
	1032	TGGACAAGCATTGAAAGATAA	
25 Exon 21; 2677 (AA 893)	1033	ACTAGAAGGTTCTGGGAAGGT	
	1034	ACTAGAAGGTGCTGGGAAGGT	SER-ALA
Intron 24; -72	1035	ACCTGGTAATCGAGAGAGTTA	
	1036	ACCTGGTAATGGAGAGAGTTA	
30 Intron 27; -182	1037	GATAGAGATGGGGTTTCACCG	
	1038	GATAGAGATGTGGTTTCACCG	
Intron 27; -168	1039	TTCACCGTGTTAGCCAGGATG	
	1040	TTCACCGTGTCAGCCAGGATG	
Intron 27; -152	1041	GGATGGTCTCAATCTGACCTT	
	1042	GGATGGTCTCGATCTGACCTT	
35 Intron 27; -135	1043	CCTTGTGATCTGCCCCGCTTG	
	1044	CCTTGTGATCCGCCCCGCTTG	
Intron 27; -98	1045	GGATTACAGGCGTGAGCCACC	
	1046	GGATTACAGGTGTGAGCCACC	
Intron 27; -87	1047	GTGAGCCACCATGCCCCGTCCT	

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		1048	GTGAGCCACCGTGCCCGTCCT
	Intron 27; -86	1049	TGAGCCACCATGCCCCGCCTA
		1050	TGAGCCACCACGCCCCGCCTA
	3' UTR; +21	1051	TATGAGATGTTAAATACTTTT
5		1052	TATGAGATGTCAAATACTTTT
	3' UTR; +79	1053	AAGCAAACACTTACAGAATTAT
		1054	AAGCAAACACACAGAATTAT
	3' UTR; +89	1055	TTACAGAATTATGAAGAGGTA
		1056	TTACAGAATTTTGAAGAGGTA
10	3' UTR; +146	1057	CAGAGACTTCGTAATTAAAGG
		1058	CAGAGACTTCATAATTAAAGG
	3' UTR; +164	1059	AGGAACAGAGTGAGAGACATC
		1060	AGGAACAGAGTGAGAGACAGAGAGACATC
			INS
			GAGAGACA
15	3' UTR; +193	1061	GAGAGAAATCATAGTTTAAAC
		1062	GAGAGAAATCGTAGTTTAAAC
	3' UTR; +252	1063	AAAAGATAAAATGTGTAATTT
		1064	AAAAGATAAACTGTGTAATTT

SEQ ID NO:1065 lists the sequence of the reference MDR1 gene (GenBank  
 20 Accession No. AC002457), promoter A and exon minus 1; SEQ ID NO:1066 (GenBank  
 Accession Nos. M57450 and AC002457), promoter B and exons 1-3; and SEQ ID  
 NO:1067 (GenBank Accession No. AC005068), exons 4-28.

### Example 23

25 This example describes the identification of variants of the known  
 lactoferrin sequence.

Using genomic DNA samples obtained from different individuals as the  
 initial template, PCR amplification of regions of the lactoferrin (LTF) gene were  
 performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 64. PCR  
 30 amplification reactions were generally performed as described in Example 1 using  
 the following primers:

**Table 64.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Promoter A	F	1068	GCTTGCCTGAGACTCTGG	1mM

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		R	1069	CGAGGACCCCGAGGA	1mM
	Exon 2	F	1070	AGGACTGTGTCTGGCT	1mM
		R	1071	GAAAATAGCAAAGTTCCCT	1mM
	Exon 3	F	1072	GGGGTCCTTGGCTCT	1mM
5		R	1073	TGTGTCTCCTCTCGTG	1mM
	Exon 5	F	1074	TTGGGAGGCACAGC	1mM
		R	1075	GGGGAACACACACTGG	1mM
	Exon 6	F	1076	CTCAAAGCAGAAGATGG	1mM
		R	1077	ATTGGTCAAGTAAGATAAAAGG	1mM
10	Exon 7	F	1078	GGGGGACTACCTTTACC	1mM
		R	1079	CAGAAGAGTTTCATTGCTT	1mM
	Exon 8	F	1080	GCCCTAAGTTGCTTGG	1mM
		R	1081	CACAGAAGACACTCACACC	1mM
	Exon 9	F	1082	AAGTGGAGGAGGAGAGG	1mM
15		R	1083	AGAGGAGTGGGAAACC	1mM
	Exon 10	F	1084	CAGCCCAGAAAGTAGG	1mM
		R	1085	GATAAAACCAACCTGTCC	1mM
	Exon 11	F	1086	GCATTTGAGTAGTTTCCAG	1mM
		R	1087	GCCAAGTGTGAAGGTC	1mM
20	Exon 12	F	1088	TGCTTTCTCGGTCTACC	1mM
		R	1089	TGGGAAGTGCTGTGC	1mM
	Exon 13	F	1090	CCTACAGTCTGAATGAAGC	1mM
		R	1091	TGCCAGCCTCCACT	1mM
	Exon 14	F	1092	AGATTGCCTGTTTCCTG	1mM
25		R	1093	CAAAATCCAAATGACACCT	1mM
	Exon 15	F	1094	CCTTGTGTAGGATGAAGC	1mM
		R	1095	AGCCAATACTCTCACCA	1mM
	Exon 16	F	1096	CACTAAGGAGGTGGAA	2mM
		R	1097	TTTGTCTTTTCTCAATGC	2mM
30	Exon 17	F	1098	GACTCTGGCTCCCTTG	1mM
		R	1099	ATTTCTCATTTTACTTCTTGC	1mM

Thermal cycling was performed as described in Example 3 except a primer annealing temperature of 58°C was used for exon 5 and 40 cycles were used for exons 5, 6 and 16. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 65.

**Table 65. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Promoter A	R	1100	CACCTCACCTGTCCTG
5 Exon 5	F	1101	ACAAATGTGCCTTCTCCT
Exon 5	R	1102	CACAGGCAACACAGGTT
Exon 8	F	1103	CCGAGGATAGATTCTGG
Exon 8	R	1104	TGCGGTGACTTGTCC
Exon 9	F	1105	GTTTCAGGGAGAGTCTGG
10 Exon 10	F	1106	GAGTTTGGATGGAGGATA
Exon 10	R	1107	CAGGACAGGCACCAA
Exon 11	F	1108	GCAACAAAGCAGTGACC
Exon 11	R	1109	CCACACAGTTAGGATCAGG
Exon 12	F	1110	GCTGGAATATCCCCAT
15 Exon 12	R	1111	AGGAGCCCGTCTGG
Exon 13	F	1112	CAGGGTGAGAATAAGTGC
Exon 13	R	1113	GAGCACAGAGATTAGTTCTCG
Exon 13	R	1114	TGTGGTGGGGACAGC
Exon 14	R	1115	ACCATCAGTGTCTGC
20 Exon 15	F	1116	GAAGCCTGTGACTGAGG
Exon 16	F	1117	GGGACCACAGTATGTGC
Exon 16	R	1118	CTGCGACATACTGTGG
Exon 16	R	1119	GTTCTAGAATGCTGTTTGG

25 Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 68.

**Table 66. Newly Identified LTF Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence	Change
Promoter 1; -470	1120	GGGGGTGGTCGGGTCATCTTT	
30	1121	GGGGGTGGTCAGGTCATCTTT	
Promoter 1; -420	1122	TGAAAGCAAACCCACCTGCCC	
	1123	TGAAAGCAAATCCACCTGCCC	
Promoter 1; -398	1124	AACTGGCTCCTAGGCACCTTC	
	1125	AACTGGCTCCAAGGCACCTTC	
35 Exon 2; 64 (AA 21)	1126	GGCTGGCCGTAGGAGAAGGAGTG	
	1127	GGCTGGCCGTAGAAGGAGTG	DEL AGG
Exon 2; 85 (AA 29)	1128	TCAGTGGTGCGCCGTATCCCA	
	1129	TCAGTGGTGACCGTATCCCA	ALA-THR



		148	
	Exon 2; 140 (AA 47)	1130	AATATGAGAAAAGTGCCTGGC
		1131	AATATGAGAAAGAGTGCCTGGC
	Intron 2; +46	1132	GAATGGAAGGGAGAGAGAAAT
		1133	GAATGGAAGGTAGAGAGAAAT
5	Intron 2; +81	1134	CACGAGCTCTCCTTACTTCCT
		1135	CACGAGCTCTTCTTACTTCCT
	Intron 2; -14	1136	CAGTCTGGCCTCTTTACTTT
		1137	CAGTCTGGCCGATCTTTACTTT
	Intron 3; +57	1138	GCCCTGAGCTGTGTGGATTAA
10		1139	GCCCTGAGCTCTGTGGATTAA
	Intron 3; +105	1140	CTGGGTACACATCACACATGTA
		1141	CTGGGTACACCACACATGTA
	Exon 5; 578 (AA 193)	1142	CGCCTGTGTGCGGGGACAGGG
		1143	CGCCTGTGTGTGGGGACAGGG
15	Intron 5; +51	1144	TGGCCTCAGGCCGGGAGGCCT
		1145	TGGCCTCAGGCCGGGAGGCCT
	Intron 5; +80	1146	GCCCCACATAGAGCCCAGCCT
		1147	GCCCCACATACAGCCCAGCCT
	Exon 6; 661	1148	GTCTGAGAGACGGGGCTGGAG
20		1149	GTCTGAGAGATGGGGCTGGAG
	Intron 7; +37	1150	TTGCTTGATATGGGGGGCAG
		1151	TTGCTTGATTTGGGGGGCAG
	Intron 8; +49	1152	TTCTACTTCCCAGCAGGTGGC
		1153	TTCTACTTCCTAGCAGGTGGC
25	Intron 8; +72	1154	TACTTTGTGGCGGTCACTCCT
		1155	TACTTTGTGGTGGTCACTCCT
	Exon 9; 1092	1156	GTGCGCGGGTCTGTGGTGTG
		1157	GTGCGCGGGTTGTGTGGTGTG
	Exon 9; 1110	1158	GTGCGGTGGGCGAGCAGGAGC
30		1159	GTGCGGTGGGTGAGCAGGAGC
	Exon 9; 1200	1160	AGGACTGCATCGCCCTGGTGC
		1161	AGGACTGCATTGCCCTGGTGC
	Intron 9; +92	1162	AGTCAAAGAGGCCACGGGGGC
		1163	AGTCAAAGAGCCCACGGGGGC
35	Intron 9; +104	1164	CACGGGGGCCCGGGTGAGGCA
		1165	CACGGGGGCCTGGGTGAGGCA
	Intron 9; -46	1166	CAGGCAGGACGGGATGCAGCC
		1167	CAGGCAGGACAGGATGCAGCC
	Intron 9; -125	1168	TCAGTTTGAACAGTCCATCTC

		149	
	1169	TCAGTTTGAATAGTCCATCTC	
Exon 10; 1248	1170	TGGATGGAGGATATGTGTACA	
	1171	TGGATGGAGGGTATGTGTACA	
Intron 11; +124	1172		
5		CTAGGAGCAATAATTTTAAGGGTGCAAATAATTC	
		ACA	
	1173	CTAGGAGCAAATAATTCACA	DEL
		TAATTTTAAGGGTGCAA	
	Intron 11; +155	1174	AATTCACAGACGAATAGTTCT
10		1175	AATTCACAGAGGAATAGTTCT
	Intron 11; -76	1176	GCCTGGGCTGCAGACAGCTCC
		1177	GCCTGGGCTGTAGACAGCTCC
	Exon 13; 1623	1178	CCAACAGCAATGAGAGATACT
		1179	CCAACAGCAACGAGAGATACT
15	Intron 13; +34	1180	CAGGATGGGGCCTTACCTCAT
		1181	CAGGATGGGGACTTACCTCAT
	Intron 13; -6	1182	TTCTGGAACATTTTAGGTGCC
		1183	TTCTGGAACAATTTAGGTGCC
	Intron 13; -26	1184	TCTGTAATTATGTGTATATTT
20		1185	TCTGTAATTACGTGTATATTT
	Intron 14; +46	1186	GAGTCTTTGGCATCACAACAC
		1187	GAGTCTTTGGTATCACAACAC
	Intron 14; -23	1188	GCGTGGATGATGCCACCTTCT
		1189	GCGTGGATGACGCCACCTTCT
25	Exon 15; 1737(AA589)	1190	ATAACAATGAGGCATGGGCTA
		1191	ATAACAATGACGCATGGGCTA
	Exon 15; 1894	1192	GAAACAGGTGCTGCTCCACCA
		1193	GAAACAGGTGTTGCTCCACCA
	Intron 15; -48	1194	CTTTAACCCATAAATTCCTCT
30		1195	CTTTAACCCACAAATTCCTCT
	Intron 16; +223	1196	CGGATAGTGACGGCACTGTCA
		1197	CGGATAGTGATGGCACTGTCA
	Intron 16; -111	1198	ACTCAGTGATGGGAGAAGGGC
		1199	ACTCAGTGATAGGAGAAGGGC
35	Intron 16; -107	1200	AGTGATGGGAGAAGGGCAGAG
		1201	AGTGATGGGAAAAGGGCAGAG

SEQ ID NO:1202 lists the sequence of the reference LTF gene (GenBank Accession No. AC002457), promoter and exon 1; SEQ ID NO:1203, exon 2; SEQ ID NO:1204, exons 3, 4 and 5; SEQ ID NO:1205, exon 6; SEQ ID NO:1206, exon 7; SEQ ID

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NO:1207, exon 8; SEQ ID NO:1208, exon 9; SEQ ID NO:1209, exon 10; SEQ ID NO:1210, exon 11; SEQ ID NO:1211, exon 12; SEQ ID NO:1212, exon 13; SEQ ID NO:1213, exon 14; SEQ ID NO:1214, exon 15; SEQ ID NO:1215, exon 16; and SEQ ID NO:1216, exon 17.

5

#### Example 24

This example describes the identification of variants of the known multidrug resistance associated protein 3 sequence.

Using genomic DNA samples obtained from different individuals as the  
10 initial template, PCR amplification of regions of the multidrug resistance associated protein 3 (MRP3) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 67. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

15 **Table 67.** PCR Primers and Mg<sup>++</sup> Concentration

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 3 & 4	F	1217	CCCAGACCTCAGTGC	1mM
	R	1218	GTGTTTGTACTTGAAGCCT	
20 Exon 5 & 6	F	1219	TCCTCATCTCTCAGAGTCCT	1mM
	R	1220	CCTCATCTGCCCTGTG	
Exon 8	F	1221	CTGTTCCCCTCCCAG	1mM
	R	1222	CTTGCCAAAGGTCACAC	
25 Exon 14 & 15	F	1223	CTAGCCCAGGATGCTG	1mM
	R	1224	CAGAACCAAGCCCTC	
Exon 17	F	1225	CCTTTGACCAAGAATGC	2mM
	R	1226	TCTGTTTCCCCAGTGC	
Exon 18	F	1227	CTGCCATCCCAAATAAC	2mM
	R	1228	TCCCCACAGGTTTCTC	
30 Exon 19	F	1229	GGTTCTGAGCAGGCTG	2mM
	R	1230	GACCCGACTATGTCCAG	
Exon 20	F	1231	TTGTTGCCCTTTCAATC	1.5mM
	R	1232	TCAGGGACAGGGGAC	
35 Exon 22	F	1233	CAGGGTTTATGGAGTCC	2mM
	R	1234	AAAGGGGCAGAATCAG	

				151	
Exon 24 & 25	F	1235	AAGGCAGCGATGTCTC		2mM
	R	1236	TTTTTCTCACAGTCCTTGA		
Exon 27 & 28	F	1237	TAGTTGGGGAGGATTGAG		2mM
	R	1238	GGCTCACTGATGGCTC		
5 Exon 30	F	1239	GCAGAAATGGGAGAAGTC		2mM
	R	1240	CCAGATCTTGGGAAACTC		
Exon 31	F	1241	TGAGCAAGTACCCAGAAG		2mM
	R	1242	GAAGTTCAGGTAACACTACAACC		

Thermal cycling was performed as described in Example 3 except exons 5, 6 and 8 were amplified for 40 cycles and exon 20 was amplified using a primer annealing temperature of 58°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used had the same sequence as the PCR primers except, or with the addition of, the primers shown in Table 68.

15

Table 68. Sequencing Primers

Region	Forward/ Reverse		SEQ ID NO:	5'-3'
20 Exon 3 & 4	F	1243	GTGGGATGGGGAGAAATGG	
	R	1244	CCATTCCCAATATGTCC	
Exon 5 & 6	F	1245	TGTAAACTGGGGCTTGGAG	
	R	1246	AGCCCCAGTTTACAGATTGTG	
Exon 14 & 15	F	1247	AGGCTACCCCATCCCTTG	
	R	1248	GAAGCAGATGTGAACAGAGG	
25 Exon 17	F	1249	CGCTACCAGCAGACTCTG	
	R	1250	GCCTGCTGGGGCACATAG	
Exon 20	F	1251	TTCTCCCTGACACTCCCAG	
	R	1252	GGGAGTGTGAGGAGAAAC	
30 Exon 22	F	1253	GGTTTATGGAGTCCCCTGT	
	R	1254	GGGCAGAATCAGAGACACG	
Exon 24 & 25	F	1255	TTCCCAGCAGGCTCTCTG	
	R	1256	CTTAGGGGAAAGGAGGGAC	
Exon 27 & 28	F	1257	CACAAAGTGCTCCAGCCAC	
	R	1258	CGCATCTCCAGGACTCTC	
35 Exon 31	F	1259	AATGACACGCCTAAGGTCAC	
	R	1260	GTCTAACTGGCTCAAACACTAGC	

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 69.

**Table 69.** Newly Identified MRP3 Gene Polymorphisms

5	Location	SEQ ID NO	Polymorphism Sequence	AA
	Change			
	Intron 3; +82	1261	GGGCTCTGAGGAGAGGGCTGG	
		1262	GGGCTCTGAGAAGAGGGCTGG	
	Intron 3; -53	1263	GAGAAATGGAGGCAGGTCCAG	
10		1264	GAGAAATGGAAGCAGGTCCAG	
	Intron 5; +73	1265	CAGCCCCCAACCCCTCCAGTT	
		1266	CAGCCCCCAACCCCTCCAGTT	
	Intron 5; -22	1267	TGATTCCTCCCGTCCTATTCTC	
		1268	TGATTCCTCCCATCCTATTCTC	
15	Intron 7; -27	1269	CCATTCCTAACCCTGCTCC	
		1270	CCATTCCTAATCCCTGCTCC	
	Intron 7; -18	1271	CCCCTGCTCCTTCCTCCCT	
		1272	CCCCTGCTTCTTCCTCCCT	
	Intron 8; +16	1273	TCCCACTCCGGCTCACTATA	
20		1274	TCCCACTCCAGCTCACTATA	
	Exon 14; 1820 (AA 607)	1275	CAATTCCTGAGCCAAGAGGAA	
		1276	CAATTCCTGAACCAAGAGGAA	SER-
	ASN			
	Intron 14; +110	1277	TTCCTCTGTTACATCTGCTT	
25		1278	TTCCTCTGTTGACATCTGCTT	
	Intron 14; +208	1279	TCCTCCCTTTCCCAAGGATC	
		1280	TCCTCCCTTTCCCAAGGATC	
	Intron 14; -79	1281	GTCTCCTTTCCCTGCCCCC	
		1282	GTCTCCTTTCCCTGCCCCC	
30	Intron 17; +34	1283	AAGAGGCTAGGGCATAGAGCT	
		1284	AAGAGGCTAGCGCATAGAGCT	
	Intron 17; +97	1285	TTCACACATTGGTGTAACGTT	
		1286	TTCACACATTAGTGTAACGTT	
	Exon 18; 2293 (AA 765)	1287	GGCTCGAGCTGTTTACAGTGA	
35		1288	GGCTCGAGCTCTTTACAGTGA	VAL-LEU
	Intron 18; -63	1289	TCTGTGGCTCCGTGCCTGTGC	
		1290	TCTGTGGCTCTGTGCCTGTGC	
	Intron 18; -28	1291	AGGGTGGTAGGGGTGAGAGCC	

		153	
		1292	AGGGTGGTAGAGGTGAGAGCC
	Intron 18; +95	1293	TAGTGTTGTGCCAGGCAGGTT
		1294	TAGTGTTGTGTCAGGCAGGTT
	Intron 18; -123	1295	CCTTTCAATCCCCCTCATTTT
5		1296	CCTTTCAATCTCCCTCATTTT
	Exon 20; 2712 (AA 904)	1297	AGCAGTTTATGAGGTGAGTTC
		1298	AGCAGTTTATAAGGTGAGTTC
	Intron 20; +29	1299	CCAGCCCTCCCGGAGGCTGTA
		1300	CCAGCCCTCCTGGAGGCTGTA
10	Intron 20; +53	1301	GGCCTCCCCAGGCCCTGCCAG
		1302	GGCCTCCCCAAGCCCTGCCAG
	Exon 22; 3039	1303	TGAGGCTGGGCGTCTATGCTG
		1304	TGAGGCTGGGTGTCTATGCTG
	Intron 22; +71	1305	CCCCCAAACCGTGCCCTTGC
15		1306	CCCCCAAAGTGTGCCCTTGC
	Intron 23; -103	1307	TGGGAGTGAGGCTGGCTGGGA
		1308	TGGGAGTGAGACTGGCTGGGA
	Intron 24; -66	1309	TCCCTCCTTTCCCTAAGCAG
		1310	TCCCTCCTTTCCCTAAGCAG
20	Intron 25; +61	1311	CACAGGTGTTCCAGGCATCTC
		1312	CACAGGTGTTTCAGGCATCTC
	Exon 27; 3942	1313	TGCATGTGCACGGTGGCGAGA
		1314	TGCATGTGCATGGTGGCGAGA
	Exon 28; 4042 (AA 1348)	1315	GGGTGAAATCCGCATTGATGG
25		1316	GGGTGAAATCTGCATTGATGG
	CYS		
	Exon 30; 4350	1317	TGGTTTTAGACGAGGCCACAG
		1318	TGGTTTTAGATGAGGCCACAG
	Intron 30; +97	1319	ACAAGGCAATGTTCCCTGGGAT
30		1320	ACAAGGCAATATTCCTGGGAT
	Exon 31; 4509	1321	TAGTAGCTGAATTTGATTCTC
		1322	TAGTAGCTGAGTTTGATTCTC

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SEQ ID NO:1323 lists the sequence of the reference MRP3 gene (GenBank Accession No. AC004590), exons 1 – 11; SEQ ID NO:1448 (GenBank Accession No. AC005921) includes exon 12 through 3' UTR.

### Example 25

This example describes the identification of variants of the known orphan nuclear receptor sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the orphan nuclear receptor (NR112) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 70. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 70. PCR Primers and Mg<sup>++</sup> Concentration**

10	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Exon 2	F	1324	GCTCCCGAGTTCACAG	1mM
		R	1325	CCACCAGCCCACACT	
	Exon 3	F	1326	CACCCTTCCCATAAAGC	1mM
15		R	1327	GCACACGGACACCAG	
	Exon 5	F	1328	ATGTGGGTGTGAATGC	1mM
		R	1329	GAAAAGGAGGGTCTTCTG	
	Exon 6	F	1330	AGCCACAGTCATCCTCA	1mM
		R	1331	ATCCCTCACCAATATCTTG	
20	Exon 7	F	1332	GAGCTACGCCAGGAT	1mM
		R	1333	GTGAAGGAAGACCAGGG	
	Exon 8	F	1334	CCCTGGTCTTCCTTCAC	1mM
		R	1335	TAGGTAGTGCTCAAAAGTGTG	
	Exon 9A	F	1336	CCTGTCTCTTGGCTGA	1mM
25		R	1337	AGCAGGGCATTGTCG	
	Exon 9B	F	1338	CAAGACAGATGGACACTG	1mM
		R	1339	CACCTGCCGATGAGT	

Thermal cycling was performed as described in Example 3 except exon 7 was amplified for 40 cycles. The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used for the sequencing had the same sequence as the PCR primers except as shown in Table 71.

**Table 71. Sequencing Primers**

35	Region	Forward/	SEQ ID	5'-3'
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155

	Reverse	NO:	
Exon 3	F	1340	TAGTGTCCCCCTCCCCGA
Exon 5	F	1341	CTGTCCACCTCCTGGCAT
	R	1342	CCAACCACCCAGTCTCCA
5 Exon 6	F	1343	TTCCTCTCGCCCCCAACTT
Exon 7	F	1344	GCAGGTTCTGGGATGGCA

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 72.

10 **Table 72.** Newly Identified NR1I2 Gene Polymorphisms

	Location	SEQ ID NO	Polymorphism Sequence
	Intron 1; -76	1345	ATGCATAGAAGGGACAGAGTG
		1346	ATGCATAGAAAGGACAGAGTG
	Exon 2; 52 (AA 18)	1347	TGTACACTGTGAGGACACAGA
15		1348	TGTACACTGTAAGGACACAGA
	Intron 2; +55	1349	ACTGGGTAACATCTCAGGGCC
		1350	ACTGGGTAACGTCTCAGGGCC
	Intron 2; +78	1351	AGCTTGACCTATCCCCCAGGT
		1352	AGCTTGACCTGTCCCCCAGGT
20	Intron 2; -29	1353	ACCCGTGCATCCCCCCTTCTG
		1354	ACCCGTGCATTCCCCCCTTCTG
	Exon 5; 696	1355	CCGACAGTGGCGGGAAAGAGA
		1356	CCGACAGTGGTGGGAAAGAGA
	Intron 5; +52	1357	GGAAGTGGCCAGGAGGTTCAA
25		1358	GGAAGTGGCCGGGAGGTTCAA
	Intron 5; -91	1359	TCTTCCTCTCGCCCCCAACTT
		1360	TCTTCCTCTCACCCCCAACTT
	Intron 5; -53	1361	CTGGTGCCGGCCTGTGGGCTG
		1362	CTGGTGCCGGTCTGTGGGCTG
30	Exon 6; 834	1363	TGCTGAAGGGGGCCGCTTTCG
		1364	TGCTGAAGGGAGCCGCTTTCG
	Intron 6; -17	1365	GCCCCCTCCATCCTGTTACCAT
		1366	GCCCCCTCCATTCTGTTACCAT
	Exon 8; 1411 (AA 370)	1367	GGAGCAATTCGCCATTACTCT
35		1368	GGAGCAATTCACCATTACTCT
	3' UTR; +15	1369	CTGCCCTTGGGTGACACCTCC
		1370	CTGCCCTTGGATGACACCTCC
	3' UTR; +370	1371	GACCAAGGATAGGCCATCTGG



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	1372	GACCAAGGATGGGCCATCTGG
3' UTR; +455	1373	CTCTAATAGTCCTGTCTCCCA
	1374	CTCTAATAGTACTGTCTCCCA
3' UTR; +500	1375	TTGTGGGCTCCAGGCCTGTAC
5	1376	TTGTGGGCTCAAGGCCTGTAC

SEQ ID NO:1377 lists the sequence of the reference NR1I2 gene, exon 2; SEQ ID NO:1378, exon 3; SEQ ID NO:1379, exon 4; SEQ ID NO:1380, exon 5; SEQ ID NO:1381, exons 6, 7 and 8; and SEQ ID NO:1382, exon 9.

#### 10 Example 26

This example describes the identification of variants of the known acetylcholine muscarinic receptor 1 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the acetylcholine muscarinic  
15 receptor 1 (CHMR1) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 73. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 73. PCR Primers and Mg<sup>++</sup> Concentration**

20 Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 1	F	1383	CTGGAGGAAGGGGCTCTC	1.1mM
	R	1384	GGGGACTGGGGTGA	

Thermal cycling was performed as described above in Example 3 except the primer  
25 annealing was performed at 60°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

The sequencing primers used for the sequencing had the same sequence as the PCR primers and those shown in Table 74.

#### 30 **Table 74. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Exon 1	F	1385	CAAAGGGGGTGGCAGCA
	F	1386	CTTCTCGCTGGTCAAGGAG

157

R	1387	CACTGTCCGCTCCCCTACCA
R	1388	GGTTGATGGTGCTGTTGACG

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 75.

5

**Table 75. Newly Identified CHMR1 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
Exon 1; 267	1389	TGCTCATGGGCCACTGGGCTC
	1390	TGCTCATGGGACACTGGGCTC
10 Exon 1; 1044	1391	GAAAGGAGCAGCTGGCCAAGC
	1392	GAAAGGAGCAACTGGCCAAGC
Exon 1; 1353	1393	GCCCTGGCTCCGTGCACCGCA
	1394	GCCCTGGCTCTGTGCACCGCA

SEQ ID NO:1395 lists the sequence of the reference CHMR1 gene (GenBank  
15 Accession No. Y00508/M35128).

#### Example 27

This example describes the identification of variants of the known acetylcholine muscarinic receptor 2 sequence.

20 Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the acetylcholine muscarinic receptor 2 (CHMR2) gene were performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 76. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

25

**Table 76. PCR Primers and Mg<sup>++</sup> Concentration**

Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
Exon 1	F	1396	CTCCACCTCAGTCAGTGC	3mM
	R	1397	CCCTGTTTGTTCCTCCTC	

30

Thermal cycling was performed as described above in Example 3 except the samples were denatured for 40 cycles. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used are shown in Table 77.

5 **Table 77. Sequencing Primers**

Region	Forward/	SEQ ID	5'-3'
	Reverse	NO:	
Exon 1	F	1398	GAATAAAAGGGATAAACG
	F	1399	CCTTGTAAGTGTGGCATTCC

10 Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 78.

**Table 78. Newly Identified CHMR2 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
15 3' UTR; +295	1400	GGGCTTCTGATTCTACAATT
	1401	GGGCTTCTGAATCTACAATT

SEQ ID NO:1402 lists the sequence of the reference CHMR2 gene (GenBank Accession No. M16404).

20 **Example 28**

This example describes the identification of variants of the known acetylcholine muscarinic receptor 3 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the acetylcholine muscarinic  
 25 receptor 3 (CHMR3) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 79. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 79. PCR Primers and Mg<sup>++</sup> Concentration**

30 Region	Forward/	SEQ ID	5'-3'	[Mg <sup>++</sup> ]
	Reverse	NO		
Exon 1	F	1403	GATGTCTGTCTGCCCTA	2mM
	R	1404	GCATCATGTTGTTCCA	

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3' UTR	F	1405	CTTGTAGAATGAGGTTGT	3.5mM
	R	1406	CAATGAACACCAGAAAG	

Thermal cycling was performed as described above in Example 3 except that the primer annealing temperature was 60°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used are shown in Table 80.

**Table 80. Sequencing Primers**

Region	Forward/ Reverse	SEQ ID NO:	5'-3'
Exon 1	F	1407	ATGTTTATTTGCTACTTG
	R	1408	ATACCTGCCATTTTGTG
3' UTR	F	1409	AATAGCAGTGACAAAACG
	F	1410	GATTTCCTGGGTCCT
	F	1411	GCAGTTCAAGTTTCGTAC
	F	1412	TGATGTCTCACCAGAGC
	R	1413	AACCACAGATTCGTAAGC
	R	1414	ACTGGGCTTATTTACG
	R	1415	TCAAGCAGTTTAGATAGC
	R	1416	GCTGATTAACAAAGGTG

Polymorphic sequences shown in **bold** were identified in the resulting nucleotide sequences listed below in Table 81.

**Table 81. Newly Identified CHMR3 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
Exon 1; 168	1417	ACGGTACCACCGATGACCCTC
	1418	ACGGTACCACTGATGACCCTC
3' UTR; +144	1419	TGTTTACTGATCCATTGAATA
	1420	TGTTTACTGACCCATTGAATA
3' UTR; +418	1421	TCCAGACCCCAAGTGGAACAC
	1422	TCCAGACCCCGAGTGGAACAC
3' UTR; +700	1423	ATTCCTGCAACATACGCTTTC
	1424	ATTCCTGCAATATACGCTTTC
3' UTR; +1094	1425	ATATATATGTGTATATATATA

160

1426 ATATATATGTATATATATATA

SEQ ID NO:1427 lists the sequence of the reference CHMR3 gene (GenBank Accession No. U29589).

### 5 Example 29

This example describes the identification of variants of the known acetylcholine muscarinic receptor 4 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the acetylcholine muscarinic  
10 receptor 4 (CHMR4) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 82. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 82. PCR Primers and Mg<sup>++</sup> Concentration**

15	Region	Forward/ Reverse	SEQ ID NO	5'-3'	[Mg <sup>++</sup> ]
	Intron 1	F	1428	GGACAACATACCAAGACC	3mM
		R	1429	ACCCACCACAAACTGC	
	Exon 1	F	1430	GCACACCGCACCTCCT	1.25mM
20		R	1431	GCTTTTCTCTCCCCTTCCT	

Thermal cycling was performed as described above in Example 3 except that the primers for exon 1 were annealed at 60°C and the other samples were annealed at 58°C. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

25 The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used were the same as the PCR primers except as shown in Table 83.

**Table 83. Sequencing Primers**

30	Region	Forward/ Reverse	SEQ ID NO:	5'-3'
	Intron 1	R	1432	GGGAAGCAAGAGGAGGA
	3' UTR	R	1433	CCGATACTGGCACAGCA

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 84.

**Table 84.** Newly Identified CHMR4 Gene Polymorphisms

5	Location	SEQ ID NO	Polymorphism Sequence
	Intron 1; -634	1434	TACATACCCCGATTATTGCCT
		1435	TACATACCCCTATTATTGCCT
	Exon 1; 1248	1436	CGCCCTACAACGTCATGGTCC
		1437	CGCCCTACAATGTCATGGTCC
10	Exon 1; 1338	1438	TCAACAGCACCATCAACCCTG
		1439	TCAACAGCACTATCAACCCTG

SEQ ID NO:1440 lists the sequence of the reference CHMR4 gene (GenBank Accession No. M16405).

#### 15 Example 30

This example describes the identification of variants of the known acetylcholine muscarinic receptor 5 sequence.

Using genomic DNA samples obtained from different individuals as the initial template, PCR amplification of regions of the acetylcholine muscarinic  
 20 receptor 5 (CHMR5) gene was performed using the primers and MgCl<sub>2</sub> concentrations listed in Table 85. PCR amplification reactions were generally performed as described in Example 1 using the following primers:

**Table 85.** PCR Primers and Mg<sup>++</sup> Concentration

25	Region	Forward/ Reverse	SEQ ID	5'-3'	[Mg <sup>++</sup> ]
			NO		
	Exon 1	F	1441	CAGCGGGAAAGGAACC	3mM
		R	1442	CTTCATAGACACATACATATTGC	

Thermal cycling was performed as described above in Example 3 except amplification of  
 30 the samples was performed for 40 cycles. The resulting PCR products were purified and sequenced using the methods described above in Example 1.

The resulting PCR products were purified and sequenced using the methods described above in Example 1. The sequencing primers used are shown in Table 86.

**Table 86. Sequencing Primers**

Region	Forward/	SEQ ID	5'-3'
	Reverse	NO:	
5 Exon 1	F	1443	
	ATGACACCCCAA ACTACC		
	R	1444	CGTTTGGTCATTTGATGG

Polymorphic sequences shown in bold were identified in the resulting nucleotide sequences listed below in Table 87.

10

**Table 87. Newly Identified CHMR5 Gene Polymorphisms**

Location	SEQ ID NO	Polymorphism Sequence
IExon 1; 1245	1445	AACCTTCAACGAAAGGCCTCA
	1446	AACCTTCAACAAAAGGCCTCA

15 SEQ ID NO:1446 lists the sequence of the reference CHMR5 gene (GenBank Accession No. M80333).

Those skilled in the art will appreciate that numerous changes and modifications may be made to the preferred embodiments of the invention and that such changes and modifications may be made without departing from the spirit of the invention. It is  
 20 therefore intended that the appended claims cover all such equivalent variations as fall within the true spirit and scope of the invention.

Claims:

1. An isolated nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4501A1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- a. a nucleic acid molecule that comprises an A for a G at position 36 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises a G for a C at position 621 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises an A for a G at position 647 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises a G for a T at position 662 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises a T for a G at position 705 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises an A for a G at position 735 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises an A for a G at position 1213 of SEQ ID NO:31 and at least 20 other bases of SEQ ID NO:31 contiguously appurtenant to said position; and
- h. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g);

(b) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4501A2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- (n) a nucleic acid molecule that comprises an A for a G at position 988 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (o) a nucleic acid molecule which comprises the deletion of a T at position 1634 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;



- (p) a nucleic acid molecule which comprises a G for an A at position 2298 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (q) a nucleic acid molecule which comprises a C for a T at position 2394 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- 5 (r) a nucleic acid molecule which comprises a G for a T at position 4079 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (s) a nucleic acid molecule which comprises a G for a C at position 4153 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- 10 (t) a nucleic acid molecule which comprises an A for a G at position 5456 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (u) a nucleic acid molecule which comprises an A for a C at position 5615 of SEQ ID NO:85 and at least 20 other bases of SEQ ID NO:85 contiguously appurtenant to said position;
- (v) a nucleic acid molecule which comprises a G for an A at position 133 of SEQ ID NO:86 and at least 20 other bases of SEQ ID NO:86 contiguously appurtenant to said position;
- 15 (w) a nucleic acid molecule which comprises a C for a G at position 291 of SEQ ID NO:86 and at least 20 other bases of SEQ ID NO:86 contiguously appurtenant to said position;
- (x) a nucleic acid molecule which comprises a C for a T at position 168 of SEQ ID NO:87 and at least 20 other bases of SEQ ID NO:87 contiguously appurtenant to said position;
- (y) a nucleic acid molecule which comprises a C for a T at position 763 of SEQ ID NO:88 and at least 20 other bases of SEQ ID NO:88 contiguously appurtenant to said position;
- 20 and
- (z) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l);
- (i) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CYP4502E1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- 25 (i) a nucleic acid molecule that comprises a G for an A at position 432 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a G for an A at position 507 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- 30 (k) a nucleic acid molecule which comprises a C for a T at position 1025 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (l) a nucleic acid molecule which comprises a T for a C at position 1075 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;

- (m) a nucleic acid molecule which comprises a G for an A at position 1085 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (n) a nucleic acid molecule which comprises a C for a G at position 1102 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position;
- (o) a nucleic acid molecule which comprises an A for a T at position 1104 of SEQ ID NO:111 and at least 20 other bases of SEQ ID NO:111 contiguously appurtenant to said position; and
- (p) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g);
- (j) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human ADRB1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- (g) a nucleic acid molecule that comprises a G for an A at position 231 of SEQ ID NO:132 and at least 20 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (h) a nucleic acid molecule which comprises a T for a C at position 401 of SEQ ID NO:132 and at least 20 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (i) a nucleic acid molecule which comprises a C for a G at position 1251 of SEQ ID NO:132 and at least 20 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (j) a nucleic acid molecule which comprises a G for a C at position 1433 of SEQ ID NO:132 and at least 20 other bases of SEQ ID NO:132 contiguously appurtenant to said position;
- (k) a nucleic acid molecule which comprises an A for a C at position 1528 of SEQ ID NO:132 and at least 20 other bases of SEQ ID NO:132 contiguously appurtenant to said position; and
- (l) a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e);
- (e) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human AHR sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a T for a C at position 2126 of SEQ ID NO:173 and at least 20 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises an A for a G at position 2159 of SEQ ID NO:173 and at least 20 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises an A for a G at position 2164 of SEQ ID NO:173 and at least 20 other bases of SEQ ID NO:173 contiguously appurtenant to said position;

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- d. a nucleic acid molecule which comprises a G for a C at position 2247 of SEQ ID NO:173 and at least 20 other bases of SEQ ID NO:173 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a C for a T at position 247 of SEQ ID NO:174 and at least 20 other bases of SEQ ID NO:174 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises the deletion of the bases AG at positions 346 and 347 of SEQ ID NO:175 and at least 20 other bases of SEQ ID NO:175 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a T for an A at position 594 of SEQ ID NO:176 and at least 20 other bases of SEQ ID NO:176 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a T for a G at position 764 of SEQ ID NO:176 and at least 20 other bases of SEQ ID NO:176 contiguously appurtenant to said position;
  - i. a nucleic acid molecule which comprises an A for a C at position 202 of SEQ ID NO:177 and at least 20 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
  - j. a nucleic acid molecule which comprises a T for a C at position 421 of SEQ ID NO:177 and at least 20 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
  - k. a nucleic acid molecule which comprises an A for a G at position 671 of SEQ ID NO:177 and at least 20 other bases of SEQ ID NO:177 contiguously appurtenant to said position;
  - l. a nucleic acid molecule which comprises an A for a G at position 718 of SEQ ID NO:177 and at least 20 other bases of SEQ ID NO:177 contiguously appurtenant to said position; and
  - m. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l);
- (f) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human ARNT sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a C for a T at position 212 of SEQ ID NO:220 and at least 20 other bases of SEQ ID NO:220 contiguously appurtenant to said position;

- b. a nucleic acid molecule which comprises an A for a G at position 471 of SEQ ID NO:221 and at least 20 other bases of SEQ ID NO:221 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a C for a G at position 160 of SEQ ID NO:222 and at least 20 other bases of SEQ ID NO:222 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a G for a T at position 142 of SEQ ID NO:225 and at least 20 other bases of SEQ ID NO:225 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises an A for a G at position 342 of SEQ ID NO:227 and at least 20 other bases of SEQ ID NO:227 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises the substitution of the bases TCACCTA for the bases ACTCTC at positions 30-35 of SEQ ID NO:232 and at least 20 other bases, alternatively at least 30 other bases of SEQ ID NO:232 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises the deletion of an A at position 62 of SEQ ID NO:233 and at least 20 other bases of SEQ ID NO:233 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a C for a T at position 330 of SEQ ID NO:234 and at least 20 other bases of SEQ ID NO:234 contiguously appurtenant to said position; and
  - i. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h);
- (g) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CTSS sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a G for an A at position 338 of SEQ ID NO:264 and at least 20 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises a T for a C at position 518 of SEQ ID NO:264 and at least 20 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises the deletion of the bases TCCC at positions 610-614 of SEQ ID NO:264 and at least 20 other bases of SEQ ID NO:264 contiguously appurtenant to said position;

- d. a nucleic acid molecule which comprises a C for a T at position 899 of SEQ ID NO:264 and at least 20 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a G for an A at position 902 of SEQ ID NO:264 and at least 20 other bases of SEQ ID NO:264 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a C for a T at position 97 of SEQ ID NO:265 and at least 20 other bases of SEQ ID NO:265 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a T for a C at position 178 of SEQ ID NO:267 and at least 20 other bases of SEQ ID NO:267 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a T for a C at position 106 of SEQ ID NO:268 and at least 20 other bases of SEQ ID NO:268 contiguously appurtenant to said position; and
  - i. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h);
- (h) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human COX2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a G for a C at position 69 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises the insertion of the bases TAG at position 180 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a C for a T at position 227 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a G for a C at position 2191 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a T for a C at position 2975 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;

- f. a nucleic acid molecule which comprises an A for a G at position 4461 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 5 g. a nucleic acid molecule which comprises the deletion of the bases TTTA at positions 4518-4521 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- h. a nucleic acid molecule which comprises a C for a T at position 4551 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 10 i. a nucleic acid molecule which comprises a C for a T at position 4719 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- j. a nucleic acid molecule which comprises a C for a T at position 4900 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 15 k. a nucleic acid molecule which comprises a C for a T at position 5310 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises a T for a C at position 6079 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 20 m. a nucleic acid molecule which comprises a C for a T at position 6620 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 25 n. a nucleic acid molecule which comprises an A for a G at position 6847 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- o. a nucleic acid molecule which comprises the deletion of the bases TTATA at positions 7180-7184 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- 30 p. a nucleic acid molecule which comprises a C for a T at position 7330 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
- q. a nucleic acid molecule which comprises a C for a G at position 7532 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position;
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- r. a nucleic acid molecule which comprises a G for an A at position 7581 of SEQ ID NO:332 and at least 20 other bases of SEQ ID NO:332 contiguously appurtenant to said position; and
  - s. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (r);
- (i) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human DBI sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a G at position 1020 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises a G for an A at position 1610 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises an A for a G at position 1652 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a T for a C at position 1681 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises an A for a G at position 1705 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises an A for a C at position 2532 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a T for a C at position 2558 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a C for a G at position 2595 of SEQ ID NO:355 and at least 20 other bases of SEQ ID NO:355 contiguously appurtenant to said position; and
  - i. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h);

(j) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human EPHX sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- 5 a. a nucleic acid molecule that comprises a G for an A at position 179 of SEQ ID NO:472 and at least 20 other bases of SEQ ID NO:472 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises a G for an A at position 232 of SEQ ID NO:473 and at least 20 other bases of SEQ ID NO:473 contiguously appurtenant to said position;
- 10 c. a nucleic acid molecule which comprises a G for an A at position 375 of SEQ ID NO:473 and at least 20 other bases of SEQ ID NO:473 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises a T for a C at position 232 of SEQ ID NO:474 and at least 20 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- 15 e. a nucleic acid molecule which comprises a T for a C at position 302 of SEQ ID NO:474 and at least 20 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises a T for a C at position 320 of SEQ ID NO:474 and at least 20 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- 20 g. a nucleic acid molecule which comprises an A for a C at position 407 of SEQ ID NO:474 and at least 20 other bases of SEQ ID NO:474 contiguously appurtenant to said position;
- 25 h. a nucleic acid molecule which comprises an A for a C at position 239 of SEQ ID NO:475 and at least 20 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- i. a nucleic acid molecule which comprises an A for a T at position 267 of SEQ ID NO:475 and at least 20 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- 30 j. a nucleic acid molecule which comprises an A for a G at position 320 of SEQ ID NO:475 and at least 20 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
- k. a nucleic acid molecule which comprises a C for a G at position 340 of SEQ ID NO:475 and at least 20 other bases of SEQ ID NO:475 contiguously appurtenant to said position;
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- l. a nucleic acid molecule which comprises a C for an A at position 235 of SEQ ID NO:476 and at least 20 other bases of SEQ ID NO:476 contiguously appurtenant to said position;
- m. a nucleic acid molecule which comprises an A for a G at position 325 of SEQ ID NO:476 and at least 20 other bases of SEQ ID NO:476 contiguously appurtenant to said position;
- n. a nucleic acid molecule which comprises a G for an A at position 204 of SEQ ID NO:477 and at least 20 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- o. a nucleic acid molecule which comprises an A for a G at position 249 of SEQ ID NO:477 and at least 20 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- p. a nucleic acid molecule which comprises an A for a G at position 322 of SEQ ID NO:477 and at least 20 other bases of SEQ ID NO:477 contiguously appurtenant to said position;
- q. a nucleic acid molecule which comprises an A for a G at position 283 of SEQ ID NO:478 and at least 20 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- r. a nucleic acid molecule which comprises a T for an A at position 689 of SEQ ID NO:478 and at least 20 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- s. a nucleic acid molecule which comprises an A for a G at position 749 of SEQ ID NO:478 and at least 20 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- t. a nucleic acid molecule which comprises a C for a T at position 807 of SEQ ID NO:478 and at least 20 other bases of SEQ ID NO:478 contiguously appurtenant to said position;
- u. a nucleic acid molecule which comprises the deletion of the bases TTT at positions 100-102 of SEQ ID NO:479 and at least 20 other bases of SEQ ID NO:479 contiguously appurtenant to said position;
- v. a nucleic acid molecule which comprises the deletion of the bases GTT at positions 103-105 of SEQ ID NO:479 and at least 20 other bases of SEQ ID NO:479 contiguously appurtenant to said position;
- w. a nucleic acid molecule which comprises a T for a C at position 212 of SEQ ID NO:480 and at least 20 other bases of SEQ ID NO:480 contiguously appurtenant to said position;

- x. a nucleic acid molecule which comprises a T for a C at position 189 of SEQ ID NO:483 and at least 20 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- y. a nucleic acid molecule which comprises the insertion of the bases TCG at position 271 of SEQ ID NO:483 and at least 20 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- z. a nucleic acid molecule which comprises a T for a C at position 298 of SEQ ID NO:483 and at least 20 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- aa. a nucleic acid molecule which comprises an A for a G at position 299 of SEQ ID NO:483 and at least 20 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- bb. a nucleic acid molecule which comprises a C for a T at position 319 of SEQ ID NO:483 and at least 20 other bases of SEQ ID NO:483 contiguously appurtenant to said position;
- cc. a nucleic acid molecule which comprises a T for a G at position 75 of SEQ ID NO:484 and at least 20 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- dd. a nucleic acid molecule which comprises an A for a G at position 80 of SEQ ID NO:484 and at least 20 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- ee. a nucleic acid molecule which comprises an A for a G at position 215 of SEQ ID NO:484 and at least 20 other bases of SEQ ID NO:484 contiguously appurtenant to said position;
- ff. a nucleic acid molecule which comprises a T for a C at position 377 of SEQ ID NO:485 and at least 20 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- gg. a nucleic acid molecule which comprises an A for a G at position 1167 of SEQ ID NO:485 and at least 20 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- hh. a nucleic acid molecule which comprises an A for a G at position 1229 of SEQ ID NO:485 and at least 20 other bases of SEQ ID NO:485 contiguously appurtenant to said position;
- ii. a nucleic acid molecule which comprises an A for a G at position 47 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;

- jj. a nucleic acid molecule which comprises a T for a C at position 286 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- 5 kk. a nucleic acid molecule which comprises an A for a C at position 509 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- ll. a nucleic acid molecule which comprises a C for an A at position 869 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- 10 mm. a nucleic acid molecule which comprises a G for an A at position 979 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- nn. a nucleic acid molecule which comprises a C for a T at position 1037 of SEQ ID NO:486 and at least 20 other bases of SEQ ID NO:486 contiguously appurtenant to said position;
- 15 oo. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (nn);
- (k) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human FLAP sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- 20 a. a nucleic acid molecule that comprises the deletion of the bases TG at positions 200-201 of SEQ ID NO:525 and at least 20 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises an A for a G at position 438 of SEQ ID NO:525 and at least 20 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- 25 c. a nucleic acid molecule which comprises a C for an A at position 461 of SEQ ID NO:525 and at least 20 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises a T for a C at position 751 of SEQ ID NO:525 and at least 20 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
- 30 e. a nucleic acid molecule which comprises an A for a C at position 862 of SEQ ID NO:525 and at least 20 other bases of SEQ ID NO:525 contiguously appurtenant to said position;
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- f. a nucleic acid molecule which comprises an A for a G at position 438 of SEQ ID NO:526 and at least 20 other bases of SEQ ID NO:526 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a C for a T at position 446 of SEQ ID NO:526 and at least 20 other bases of SEQ ID NO:526 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a T for a G at position 301 of SEQ ID NO:527 and at least 20 other bases of SEQ ID NO:527 contiguously appurtenant to said position; and
  - i. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (h);
- (l) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human GST12 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a C for a T at position 1146 of SEQ ID NO:545 and at least 20 other bases of SEQ ID NO:545 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises a G for a C at position 241 of SEQ ID NO:546 and at least 20 other bases of SEQ ID NO:546 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a C for a T at position 101 of SEQ ID NO:547 and at least 20 other bases of SEQ ID NO:547 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises an A for a G at position 385 of SEQ ID NO:547 and at least 20 other bases of SEQ ID NO:547 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a G for a T at position 423 of SEQ ID NO:547 and at least 20 other bases of SEQ ID NO:547 contiguously appurtenant to said position; and
  - f. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e);
- (m) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human HNMT sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- a. a nucleic acid molecule that comprises a C for a G at position 723 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises the deletion of the base A at position 755 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises a G for an A at position 893 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises a C for a T at position 1002 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises a T for a C at position 1054 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises a C for a T at position 1088 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises an A for a G at position 1320 of SEQ ID NO:592 and at least 20 other bases of SEQ ID NO:592 contiguously appurtenant to said position;
- h. a nucleic acid molecule which comprises an A for a G at position 97 of SEQ ID NO:593 and at least 20 other bases of SEQ ID NO:593 contiguously appurtenant to said position;
- i. a nucleic acid molecule which comprises an A for a C at position 509 of SEQ ID NO:594 and at least 20 other bases of SEQ ID NO:594 contiguously appurtenant to said position;
- j. a nucleic acid molecule which comprises a T for a C at position 271 of SEQ ID NO:595 and at least 20 other bases of SEQ ID NO:595 contiguously appurtenant to said position;
- k. a nucleic acid molecule which comprises the deletion of the bases AA at positions 434-435 of SEQ ID NO:595 and at least 20 other bases of SEQ ID NO:595 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises an A for a G at position 663 of SEQ ID NO:597 and at least 20 other bases of SEQ ID NO:597 contiguously appurtenant to said position; and

- m. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l);
- (n) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human KLK2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- 5
- a. a nucleic acid molecule that comprises an A for a G at position 281 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- 10
- b. a nucleic acid molecule which comprises a G for a C at position 630 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises a G for an A at position 683 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- 15
- d. a nucleic acid molecule which comprises an A for a G at position 1771 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises a T for a C at position 3689 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- 20
- f. a nucleic acid molecule which comprises a G for an A at position 3865 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises an A for a T at position 3906 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- 25
- h. a nucleic acid molecule which comprises an A for a C at position 4160 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position;
- 30
- i. a nucleic acid molecule which comprises a T for a C at position 5571 of SEQ ID NO:634 and at least 20 other bases of SEQ ID NO:634 contiguously appurtenant to said position; and
- j. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (i);

(o) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human NNMT sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- 5 a. a nucleic acid molecule that comprises a G for an A at position 330 of SEQ ID NO:655 and at least 20 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises a T for an A at position 394 of SEQ ID NO:655 and at least 20 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- 10 c. a nucleic acid molecule which comprises a T for a C at position 707 of SEQ ID NO:655 and at least 20 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises a C for a T at position 928 of SEQ ID NO:655 and at least 20 other bases of SEQ ID NO:655 contiguously appurtenant to said position;
- 15 e. a nucleic acid molecule which comprises a G for an A at position 643 of SEQ ID NO:656 and at least 20 other bases of SEQ ID NO:656 contiguously appurtenant to said position; and
- f. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e);
- 20

(p) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human NQO2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

- 25 a. a nucleic acid molecule that comprises a G for an A at position 1318 of SEQ ID NO:721 and at least 20 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- b. a nucleic acid molecule which comprises an A for a C at position 1507 of SEQ ID NO:721 and at least 20 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- 30 c. a nucleic acid molecule which comprises a T for a C at position 1536 of SEQ ID NO:721 and at least 20 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises an A for a C at position 1541 of SEQ ID NO:721 and at least 20 other bases of SEQ ID NO:721 contiguously appurtenant to said position;
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- e. a nucleic acid molecule which comprises a T for a C at position 218 of SEQ ID NO:722 and at least 20 other bases of SEQ ID NO:722 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises a C for a T at position 298 of SEQ ID NO:722 and at least 20 other bases of SEQ ID NO:722 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises a G for an A at position 418 of SEQ ID NO:722 and at least 20 other bases of SEQ ID NO:722 contiguously appurtenant to said position;
- h. a nucleic acid molecule which comprises a T for a C at position 326 of SEQ ID NO:723 and at least 20 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- i. a nucleic acid molecule which comprises a G for an A at position 280 of SEQ ID NO:723 and at least 20 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- j. a nucleic acid molecule which comprises a C for a T at position 372 of SEQ ID NO:723 and at least 20 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- k. a nucleic acid molecule which comprises a C for a T at position 441 of SEQ ID NO:723 and at least 20 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises a G for an A at position 464 of SEQ ID NO:723 and at least 20 other bases of SEQ ID NO:723 contiguously appurtenant to said position;
- m. a nucleic acid molecule which comprises the deletion of the base G at position 80 of SEQ ID NO:724 and at least 20 other bases of SEQ ID NO:794 contiguously appurtenant to said position;
- n. a nucleic acid molecule which comprises an A for a G at position 202 of SEQ ID NO:725 and at least 20 other bases of SEQ ID NO:725 contiguously appurtenant to said position;
- o. a nucleic acid molecule which comprises a T for a C at position 277 of SEQ ID NO:725 and at least 20 other bases of SEQ ID NO:725 contiguously appurtenant to said position;
- p. a nucleic acid molecule which comprises an A for a T at position 310 of SEQ ID NO:725 and at least 20 other bases of SEQ ID NO:725 contiguously appurtenant to said position;



- q. a nucleic acid molecule which comprises a G for an A at position 78 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- 5 r. a nucleic acid molecule which comprises a T for a C at position 214 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- s. a nucleic acid molecule which comprises a G for an A at position 379 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- 10 t. a nucleic acid molecule which comprises a G for an A at position 381 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- u. a nucleic acid molecule which comprises the insertion of the bases GC at position 381 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- 15 v. a nucleic acid molecule which comprises the insertion of the bases GCAC at position 381 of SEQ ID NO:726 and at least 20 other bases of SEQ ID NO:726 contiguously appurtenant to said position;
- w. a nucleic acid molecule which comprises a C for a G at position 322 of SEQ ID NO:727 and at least 20 other bases of SEQ ID NO:727 contiguously appurtenant to said position; and
- 20 x. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (w);
- (q) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human STM sequence, wherein said nucleic acid molecule is selected from the group consisting of:
  - 25 a. a nucleic acid molecule that comprises a C for a G at position 835 of SEQ ID NO:745 and at least 20 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
  - 30 b. a nucleic acid molecule which comprises a T for a C at position 841 of SEQ ID NO:745 and at least 20 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a G for an A at position 4465 of SEQ ID NO:745 and at least 20 other bases of SEQ ID NO:745 contiguously appurtenant to said position;
  - 35

- d. a nucleic acid molecule which comprises the deletion of the bases AATT at positions 7930-7933 of SEQ ID NO:745 and at least 20 other bases of SEQ ID NO:745 contiguously appurtenant to said position; and
  - e. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (d);
- (r) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human UGT2B4 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a G at position 5227 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises a T for a C at position 5229 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises an A for a G at position 5671 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a C for an A at position 5827 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a T for a C at position 5919 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a C for a T at position 5994 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a G for an A at position 6101 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a T for an A at position 6220 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - i. a nucleic acid molecule which comprises a G for a C at position 6299 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;

- j. a nucleic acid molecule which comprises a T for a C at position 6539 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - k. a nucleic acid molecule which comprises a T for an A at position 6866 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position;
  - l. a nucleic acid molecule which comprises a T for a G at position 6921 of SEQ ID NO:789 and at least 20 other bases of SEQ ID NO:789 contiguously appurtenant to said position; and
  - m. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l);
- (s) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human UGT2B7 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a C for a T at position 33 of SEQ ID NO:826 and at least 20 other bases, alternatively at least 30 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises an A for a G at position 247 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a T for a C at position 412 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises an A for a G at position 613 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a G for an A at position 820 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a C for a T at position 986 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises an A for a G at position 1009 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;

- h. a nucleic acid molecule which comprises a C for a T at position 1022 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position;
  - i. a nucleic acid molecule which comprises a T for a C at position 1115 of SEQ ID NO:826 and at least 20 other bases of SEQ ID NO:826 contiguously appurtenant to said position; and
  - j. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (i);
- (t) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human UGT2B15 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a G at position 95 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises an A for a C at position 107 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a T for a C at position 365 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a C for an A at position 562 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a G for a C at position 642 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a T for a G at position 686 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a C for a T at position 991 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a G for an A at position 996 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;

- i. a nucleic acid molecule which comprises a T for an A at position 998 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - j. a nucleic acid molecule which comprises a T for a C at position 1007 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - k. a nucleic acid molecule which comprises a C for a T at position 1062 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - l. a nucleic acid molecule which comprises an A for a G at position 1111 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - m. a nucleic acid molecule which comprises a T for a C at position 1126 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position;
  - n. a nucleic acid molecule which comprises an A for a G at position 1287 of SEQ ID NO:867 and at least 20 other bases of SEQ ID NO:867 contiguously appurtenant to said position; and
  - o. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (n);
- (u) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human uPA sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a C at position 1209 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises an A for a C at position 1312 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises an A for a G at position 1775 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a T for a C at position 3005 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;

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- e. a nucleic acid molecule which comprises a C for a T at position 3635 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a C for an A at position 3652 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a T for a C at position 3783 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises a C for a T at position 4662 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - i. a nucleic acid molecule which comprises a G for an A at position 4818 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - j. a nucleic acid molecule which comprises a C for a T at position 6398 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - k. a nucleic acid molecule which comprises a T for a C at position 7011 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position;
  - l. a nucleic acid molecule which comprises the deletion of the base G at position 7103 of SEQ ID NO:918 and at least 20 other bases of SEQ ID NO:918 contiguously appurtenant to said position; and
  - m. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (l);
- (v) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human MDR1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a C for a T at position 614 of SEQ ID NO:1065 and at least 20 other bases of SEQ ID NO:1065 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises a C for a T at position 794 of SEQ ID NO:1065 and at least 20 other bases of SEQ ID NO:1065 contiguously appurtenant to said position;

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- c. a nucleic acid molecule which comprises an A for a G at position 370 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises an A for a G at position 672 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises a C for a T at position 812 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises a G for an A at position 2723 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises a G for an A at position 2783 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- h. a nucleic acid molecule which comprises a T for a C at position 7177 of SEQ ID NO:1066 and at least 20 other bases of SEQ ID NO:1066 contiguously appurtenant to said position;
- i. a nucleic acid molecule which comprises a T for a G at position 24899 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- j. a nucleic acid molecule which comprises a G for a T at position 25052 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- k. a nucleic acid molecule which comprises a C for a T at position 28523 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises a G for an A at position 33860 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- m. a nucleic acid molecule which comprises a G for an A at position 41131 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- n. a nucleic acid molecule which comprises a G for a T at position 44550 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;

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- o. a nucleic acid molecule which comprises a C for a T at position 44884 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- p. a nucleic acid molecule which comprises a T for a C at position 45042 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- q. a nucleic acid molecule which comprises a C for a T at position 45342 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- r. a nucleic acid molecule which comprises a T for a C at position 4539 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- s. a nucleic acid molecule which comprises an A for a G at position 45859 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- t. a nucleic acid molecule which comprises an A for a G at position 49344 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- u. a nucleic acid molecule which comprises a G for an A at position 50419 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- v. a nucleic acid molecule which comprises an A for a T at position 50818 of SEQ ID NO:1067 and at least 20 other bases of SEQ ID NO:1067 contiguously appurtenant to said position;
- w. a nucleic acid molecule which comprises an A for a G at position 25101 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- x. a nucleic acid molecule which comprises a C for a G at position 25154 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- y. a nucleic acid molecule which comprises an A for a G at position 25395 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;



- z. a nucleic acid molecule which comprises a T for a C at position 33205 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 5 aa. a nucleic acid molecule which comprises a G for a C at position 49034 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 10 bb. a nucleic acid molecule which comprises a T for a G at position 59903 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 15 cc. a nucleic acid molecule which comprises a C for a T at position 59917 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 20 dd. a nucleic acid molecule which comprises a G for an A at position 59933 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 25 ee. a nucleic acid molecule which comprises a C for a T at position 59950 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 30 ff. a nucleic acid molecule which comprises a T for a C at position 59987 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 35 gg. a nucleic acid molecule which comprises a G for an A at position 59998 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- hh. a nucleic acid molecule which comprises a C for a T at position 59999 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;

- ii. a nucleic acid molecule which comprises a C for a T at position 60312 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 5    jj. a nucleic acid molecule which comprises the deletion of the bases TT at positions 60316 and 60317 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 10    kk. a nucleic acid molecule which comprises a T for an A at position 60380 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 15    ll. a nucleic acid molecule which comprises an A for a G at position 60437 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 20    mm. a nucleic acid molecule which comprises the insertion of the bases GAGAGACA at position 60455 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 25    nn. a nucleic acid molecule which comprises a G for an A at position 60484 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;
- 30    oo. a nucleic acid molecule which comprises a C for an A at position 60543 of SEQ ID NO:1449 and at least 20 other bases, alternatively at least 30 other bases, at least 40 other bases or at least 50 other bases of SEQ ID NO:1449 contiguously appurtenant to said position;and
- 35    pp. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (oo);
- (w) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human LTF sequence, wherein said nucleic acid molecule is selected from the group consisting of:
  - a. a nucleic acid molecule that comprises an A for a G at position 48 of SEQ ID NO:1202 and at least 20 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;

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- b. a nucleic acid molecule which comprises a T for a C at position 98 of SEQ ID NO:1202 and at least 20 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises an A for a T at position 120 of SEQ ID NO:1202 and at least 20 other bases of SEQ ID NO:1202 contiguously appurtenant to said position;
- d. a nucleic acid molecule which comprises the deletion of the bases AGG at positions 21-23 of SEQ ID NO:1203 and at least 20 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises an A for a G at position 45 of SEQ ID NO:1203 and at least 20 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- f. a nucleic acid molecule which comprises a G for an A at position 100 of SEQ ID NO:1203 and at least 20 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- g. a nucleic acid molecule which comprises a T for a G at position 213 of SEQ ID NO:1203 and at least 20 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- h. a nucleic acid molecule which comprises a T for a G at position 248 of SEQ ID NO:1203 and at least 20 other bases of SEQ ID NO:1203 contiguously appurtenant to said position;
- i. a nucleic acid molecule which comprises the insertion of the bases GA at position 114 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- j. a nucleic acid molecule which comprises a C for a G at position 293 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- k. a nucleic acid molecule which comprises a C for a T at position 341 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises a T for a C at position 1151 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- m. a nucleic acid molecule which comprises a G for a C at position 1274 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;

- n. a nucleic acid molecule which comprises a C for a G at position 1303 of SEQ ID NO:1204 and at least 20 other bases of SEQ ID NO:1204 contiguously appurtenant to said position;
- 5 o. a nucleic acid molecule which comprises a T for a C at position 209 of SEQ ID NO:1205 and at least 20 other bases of SEQ ID NO:1205 contiguously appurtenant to said position;
- p. a nucleic acid molecule which comprises a T for an A at position 367 of SEQ ID NO:1206 and at least 20 other bases of SEQ ID NO:1206 contiguously appurtenant to said position;
- 10 q. a nucleic acid molecule which comprises a T for a C at position 409 of SEQ ID NO:1207 and at least 20 other bases of SEQ ID NO:1207 contiguously appurtenant to said position;
- r. a nucleic acid molecule which comprises a T for a C at position 432 of SEQ ID NO:1207 and at least 20 other bases of SEQ ID NO:1207 contiguously appurtenant to said position;
- 15 s. a nucleic acid molecule which comprises a T for a C at position 108 of SEQ ID NO:1208 and at least 20 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- t. a nucleic acid molecule which comprises a T for a C at position 126 of SEQ ID NO:1208 and at least 20 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- 20 u. a nucleic acid molecule which comprises a T for a C at position 216 of SEQ ID NO:1208 and at least 20 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- 25 v. a nucleic acid molecule which comprises a C for a G at position 320 of SEQ ID NO:1208 and at least 20 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- w. a nucleic acid molecule which comprises a T for a C at position 332 of SEQ ID NO:1208 and at least 20 other bases of SEQ ID NO:1208 contiguously appurtenant to said position;
- 30 x. a nucleic acid molecule which comprises an A for a G at position 120 of SEQ ID NO:1209 and at least 20 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
- y. a nucleic acid molecule which comprises a T for a C at position 41 of SEQ ID NO:1209 and at least 20 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
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- z. a nucleic acid molecule which comprises a G for an A at position 202 of SEQ ID NO:1209 and at least 20 other bases of SEQ ID NO:1209 contiguously appurtenant to said position;
- 5 aa. a nucleic acid molecule which comprises the deletion of the bases TAATTTTAAGGGTGCAA at positions 359-375 of SEQ ID NO:1210 and at least 20 other bases of SEQ ID NO:1210 contiguously appurtenant to said positions;
- bb. a nucleic acid molecule which comprises a G for a C at position 388 of SEQ ID NO:1210 and at least 20 other bases of SEQ ID NO:1210 contiguously appurtenant to said position;
- 10 cc. a nucleic acid molecule which comprises a T for a C at position 44 of SEQ ID NO:1211 and at least 20 other bases of SEQ ID NO:1211 contiguously appurtenant to said position;
- dd. a nucleic acid molecule which comprises a C for a T at position 285 of SEQ ID NO:1212 and at least 20 other bases of SEQ ID NO:1212 contiguously appurtenant to said position;
- 15 ee. a nucleic acid molecule which comprises an A for a C at position 351 of SEQ ID NO:1212 and at least 20 other bases of SEQ ID NO:1212 contiguously appurtenant to said position;
- ff. a nucleic acid molecule which comprises an A for a T at position 222 of SEQ ID NO:1213 and at least 20 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- 20 gg. a nucleic acid molecule which comprises a C for a T at position 202 of SEQ ID NO:1213 and at least 20 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- 25 hh. a nucleic acid molecule which comprises a T for a C at position 341 of SEQ ID NO:1213 and at least 20 other bases of SEQ ID NO:1213 contiguously appurtenant to said position;
- ii. a nucleic acid molecule which comprises a C for a T at position 98 of SEQ ID NO:1214 and at least 20 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
- 30 jj. a nucleic acid molecule which comprises a C for a G at position 134 of SEQ ID NO:1214 and at least 20 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
- kk. a nucleic acid molecule which comprises a T for a C at position 291 of SEQ ID NO:1214 and at least 20 other bases of SEQ ID NO:1214 contiguously appurtenant to said position;
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- ll. a nucleic acid molecule which comprises a C for a T at position 63 of SEQ ID NO:1215 and at least 20 other bases of SEQ ID NO:1215 contiguously appurtenant to said position;
- mm. a nucleic acid molecule which comprises a T for a C at position 523 of SEQ ID NO:1215 and at least 20 other bases of SEQ ID NO:1215 contiguously appurtenant to said position;
- nn. a nucleic acid molecule which comprises an A for a G at position 61 of SEQ ID NO:1216 and at least 20 other bases of SEQ ID NO:1216 contiguously appurtenant to said position;
- oo. a nucleic acid molecule which comprises an A for a G at position 65 of SEQ ID NO:1216 and at least 20 other bases of SEQ ID NO:1216 contiguously appurtenant to said position; and
- pp. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (oo);
- (x) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human MRP3 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
  - a. a nucleic acid molecule that comprises an A for a G at position 23544 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises an A for a G at position 23627 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises an A for a C at position 24912 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises an A for a G at position 25045 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a T for a C at position 27526 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a T for a C at position 27535 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position;

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- g. a nucleic acid molecule which comprises an A for a G at position 759 of SEQ ID NO:1323 and at least 20 other bases of SEQ ID NO:1323 contiguously appurtenant to said position; and
  - h. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (g);
- (y) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human NR112 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a G at position 248 of SEQ ID NO:1377 and at least 20 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
  - b. a nucleic acid molecule which comprises an A for a G at position 397 of SEQ ID NO:1377 and at least 20 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
  - c. a nucleic acid molecule which comprises a G for an A at position 597 of SEQ ID NO:1377 and at least 20 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
  - d. a nucleic acid molecule which comprises a G for an A at position 620 of SEQ ID NO:1377 and at least 20 other bases of SEQ ID NO:1377 contiguously appurtenant to said position;
  - e. a nucleic acid molecule which comprises a T for a C at position 224 of SEQ ID NO:1378 and at least 20 other bases of SEQ ID NO:1378 contiguously appurtenant to said position;
  - f. a nucleic acid molecule which comprises a T for a C at position 467 of SEQ ID NO:1380 and at least 20 other bases of SEQ ID NO:1380 contiguously appurtenant to said position;
  - g. a nucleic acid molecule which comprises a G for an A at position 617 of SEQ ID NO:1380 and at least 20 other bases of SEQ ID NO:1380 contiguously appurtenant to said position;
  - h. a nucleic acid molecule which comprises an A for a G at position 208 of SEQ ID NO:1381 and at least 20 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
  - i. a nucleic acid molecule which comprises a T for a C at position 248 of SEQ ID NO:1381 and at least 20 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;

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- j. a nucleic acid molecule which comprises an A for a G at position 340 of SEQ ID NO:1381 and at least 20 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- 5 k. a nucleic acid molecule which comprises a T for a C at position 666 of SEQ ID NO:1381 and at least 20 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- l. a nucleic acid molecule which comprises an A for a G at position 1082 of SEQ ID NO:1381 and at least 20 other bases of SEQ ID NO:1381 contiguously appurtenant to said position;
- 10 m. a nucleic acid molecule which comprises an A for a G at position 402 of SEQ ID NO:1382 and at least 20 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- n. a nucleic acid molecule which comprises a G for an A at position 757 of SEQ ID NO:1382 and at least 20 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- 15 o. a nucleic acid molecule which comprises an A for a C at position 832 of SEQ ID NO:1382 and at least 20 other bases of SEQ ID NO:1382 contiguously appurtenant to said position;
- p. a nucleic acid molecule which comprises an A for a C at position 887 of SEQ ID NO:1382 and at least 20 other bases of SEQ ID NO:1382 contiguously appurtenant to said position; and
- 20 q. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (p);
- (z) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR1 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- 25 a. a nucleic acid molecule that comprises an A for a C at position 717 of SEQ ID NO:1395 and at least 20 other bases of SEQ ID NO:1395 contiguously appurtenant to said position;
- 30 b. a nucleic acid molecule which comprises an A for a G at position 1494 of SEQ ID NO:1395 and at least 20 other bases of SEQ ID NO:1395 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises a T for a C at position 1803 of SEQ ID NO:1395 and at least 20 other bases of SEQ ID NO:1395 contiguously appurtenant to said position; and
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- d. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (c);
- (aa) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR2 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- 5 a. a nucleic acid molecule that comprises an A for a T at position 1890 of SEQ ID NO:1402 and at least 20 other bases of SEQ ID NO:1402 contiguously appurtenant to said position; and
- b. a nucleic acid which is fully complementary to a nucleic acid molecule of (a);
- 10 (bb) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR3 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a T for a C at position 369 of SEQ ID NO1427 and at least 20 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- 15 b. a nucleic acid molecule which comprises a C for a T at position 2118 of SEQ ID NO1427 and at least 20 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises a G for an A at position 2392 of SEQ ID NO1427 and at least 20 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- 20 d. a nucleic acid molecule which comprises a T for a C at position 2674 of SEQ ID NO1427 and at least 20 other bases of SEQ ID NO1427 contiguously appurtenant to said position;
- e. a nucleic acid molecule which comprises an A for a G at position 2601 of SEQ ID NO1427 and at least 20 other bases of SEQ ID NO1427 contiguously appurtenant to said position; and
- 25 f. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (e);
- 30 (cc) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR4 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises a T for a G at position 138 of SEQ ID NO:1440 and at least 20 other bases of SEQ ID NO:1440 contiguously appurtenant to said position;
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- b. a nucleic acid molecule which comprises a T for a C at position 2048 of SEQ ID NO:1440 and at least 20 other bases of SEQ ID NO:1440 contiguously appurtenant to said position;
- c. a nucleic acid molecule which comprises a T for a C at position 2138 of SEQ ID NO:1440 and at least 20 other bases of SEQ ID NO:1440 contiguously appurtenant to said position; and
- d. a nucleic acid which is fully complementary to a nucleic acid molecule of (a) through (c); and,
- (dd) an isolated nucleic acid molecule that comprises at least one base variation from that of a known human CHMR5 sequence, wherein said nucleic acid molecule is selected from the group consisting of:
- a. a nucleic acid molecule that comprises an A for a G at position 1493 of SEQ ID NO:1447 and at least 20 other bases of SEQ ID NO:1447 contiguously appurtenant to said position; and
- b. a nucleic acid which is fully complementary to a nucleic acid molecule of (a).
2. An isolated nucleic acid molecule, as claimed in Claim 1, wherein said nucleic acid molecule is less than about 5 kilobases in length.
3. An isolated nucleic acid molecule, as claimed in Claim 1, wherein said nucleic acid molecule is less than about 70 nucleotides in length.
4. A method of genotyping an individual comprising:
- a. obtaining a nucleic acid molecule sample from an individual;
- b. determining whether said nucleic acid molecule sample comprises a sequence of a nucleic acid molecule of Claim 1.
5. A method of genotyping an individual, as claimed in Claim 4, wherein said nucleic acid molecule sample is genomic DNA.
6. A method of genotyping an individual, as claimed in Claim 4, wherein said determining comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence and the corresponding wildtype sequence.
7. A method of genotyping an individual, as claimed in Claim 4, wherein said step of determining comprises amplifying a selected region of the nucleic acid molecule of the individual.

8. An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of

- 5           a. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, and complementary sequences thereof;
- 10          b. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 62, SEQ ID NO: 64, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 72, SEQ ID NO: 74, SEQ ID NO: 76, SEQ ID NO: 78, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, and complementary sequences thereof;
- 15          c. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 98, SEQ ID NO: 100, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 108, SEQ ID NO: 110, and complementary sequences thereof;
- 20          d. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, and complementary sequences thereof;
- 25          e. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 150, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 156, SEQ ID NO: 158, SEQ ID NO: 160, SEQ ID NO: 162, SEQ ID NO: 164, SEQ ID NO: 166, SEQ ID NO: 168, SEQ ID NO: 170, SEQ ID NO: 172, and complementary sequences thereof;
- 30          f. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 205, SEQ ID NO: 207, SEQ ID NO: 209, SEQ ID NO: 211, SEQ ID NO: 213, SEQ ID NO: 215, SEQ ID NO: 217, SEQ ID NO: 219, and complementary sequences thereof;
- 35          g. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 249, SEQ ID NO: 251, SEQ ID NO: 253, SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, and complementary sequences thereof;
- h. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 297, SEQ ID NO: 299, SEQ ID NO: 301, SEQ ID NO: 303, SEQ ID NO: 305, SEQ ID NO: 307, SEQ ID NO: 309, SEQ ID NO: 311, SEQ ID NO: 313, SEQ ID NO: 315, SEQ ID NO: 317, SEQ ID NO: 319, SEQ ID NO: 321, SEQ ID NO: 323, SEQ ID NO: 325, SEQ ID NO: 327, SEQ ID NO: 329, SEQ ID NO: 331, and complementary sequences thereof;

- i. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 340, SEQ ID NO: 342, SEQ ID NO: 344, SEQ ID NO: 346, SEQ ID NO: 348, SEQ ID NO: 350, SEQ ID NO: 352, SEQ ID NO: 354, and complementary sequences thereof;
- 5 j. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 393, SEQ ID NO: 395, SEQ ID NO: 397, SEQ ID NO: 399, SEQ ID NO: 401, SEQ ID NO: 403, SEQ ID NO: 405, SEQ ID NO: 407, SEQ ID NO: 409, SEQ ID NO: 411, SEQ ID NO: 413, SEQ ID NO: 415, SEQ ID NO: 417, SEQ ID NO: 419, SEQ ID NO: 421, SEQ ID NO: 423, SEQ ID NO: 425, SEQ ID NO: 427, SEQ ID NO: 429, SEQ ID NO: 431, SEQ ID NO: 433, SEQ ID NO: 435, SEQ ID NO: 437, SEQ ID NO: 439, SEQ ID NO: 441, SEQ ID NO: 443, SEQ ID NO: 445, SEQ ID NO: 447, SEQ ID NO: 449, SEQ ID NO: 451, SEQ ID NO: 453, SEQ ID NO: 455, SEQ ID NO: 457, SEQ ID NO: 459, SEQ ID NO: 461, SEQ ID NO: 463, SEQ ID NO: 465, SEQ ID NO: 467, SEQ ID NO: 469, SEQ ID NO: 471, and  
10 complementary sequences thereof;
- k. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 506, SEQ ID NO: 508, SEQ ID NO: 510, SEQ ID NO: 512, SEQ ID NO: 514, SEQ ID NO: 516, SEQ ID NO: 518, SEQ ID NO: 520, SEQ ID NO: 522, SEQ ID NO: 524, and complementary sequences thereof;
- 20 l. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 536, SEQ ID NO: 538, SEQ ID NO: 540, SEQ ID NO: 542, SEQ ID NO: 544, and complementary sequences thereof;
- m. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 567, SEQ ID NO: 569, SEQ ID NO: 571, SEQ ID NO: 573, SEQ ID NO: 575, SEQ ID NO: 577, SEQ ID NO: 579, SEQ ID NO: 581, SEQ ID NO: 583, SEQ ID NO: 585, SEQ ID NO: 587, SEQ ID NO: 589, SEQ ID NO: 591, and complementary  
25 sequences thereof;
- n. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 617, SEQ ID NO: 619, SEQ ID NO: 621, SEQ ID NO: 623, SEQ ID NO: 625, SEQ ID NO: 627, SEQ ID NO: 629, SEQ ID NO: 631, SEQ ID NO: 633, and  
30 complementary sequences thereof;
- o. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 646, SEQ ID NO: 648, SEQ ID NO: 650, SEQ ID NO: 652, SEQ ID NO: 654, and complementary sequences thereof;
- 35 p. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 676, SEQ ID NO: 678, SEQ ID NO: 680, SEQ ID NO: 682, SEQ ID NO: 684, SEQ ID

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NO: 686, SEQ ID NO: 688, SEQ ID NO: 690, SEQ ID NO: 692, SEQ ID NO: 694, SEQ ID NO: 696, SEQ ID NO: 698, SEQ ID NO: 700, SEQ ID NO: 702, SEQ ID NO: 704, SEQ ID NO: 706, SEQ ID NO: 708, SEQ ID NO: 710, SEQ ID NO: 712, SEQ ID NO: 714, SEQ ID NO: 716, SEQ ID NO: 718, SEQ ID NO: 720, and complementary sequences thereof;

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q. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 738, SEQ ID NO: 740, SEQ ID NO: 742, SEQ ID NO: 744, and complementary sequences thereof;

r. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 766, SEQ ID NO: 768, SEQ ID NO: 770, SEQ ID NO: 772, SEQ ID NO: 774, SEQ ID NO: 776, SEQ ID NO: 778, SEQ ID NO: 780, SEQ ID NO: 782, SEQ ID NO: 784, SEQ ID NO: 786, SEQ ID NO: 788, and complementary sequences thereof;

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s. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 809, SEQ ID NO: 811, SEQ ID NO: 813, SEQ ID NO: 815, SEQ ID NO: 817, SEQ ID NO: 819, SEQ ID NO: 821, SEQ ID NO: 823, SEQ ID NO: 825, and complementary sequences thereof;

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t. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 840, SEQ ID NO: 842, SEQ ID NO: 844, SEQ ID NO: 846, SEQ ID NO: 848, SEQ ID NO: 850, SEQ ID NO: 852, SEQ ID NO: 854, SEQ ID NO: 856, SEQ ID NO: 858, SEQ ID NO: 860, SEQ ID NO: 862, SEQ ID NO: 864, SEQ ID NO: 866, and complementary sequences thereof;

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u. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 895, SEQ ID NO: 897, SEQ ID NO: 899, SEQ ID NO: 901, SEQ ID NO: 903, SEQ ID NO: 905, SEQ ID NO: 907, SEQ ID NO: 909, SEQ ID NO: 911, SEQ ID NO: 913, SEQ ID NO: 915, SEQ ID NO: 917, and complementary sequences thereof;

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v. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 982, SEQ ID NO: 984, SEQ ID NO: 986, SEQ ID NO: 988, SEQ ID NO: 990, SEQ ID NO: 992, SEQ ID NO: 994, SEQ ID NO: 996, SEQ ID NO: 998, SEQ ID NO: 1000, SEQ ID NO: 1002, SEQ ID NO: 1004, SEQ ID NO: 1006, SEQ ID NO: 1008, SEQ ID NO: 1010, SEQ ID NO: 1012, SEQ ID NO: 1014, SEQ ID NO: 1016, SEQ ID NO: 1018, SEQ ID NO: 1020, SEQ ID NO: 1022, SEQ ID NO: 1024, SEQ ID NO: 1026, SEQ ID NO: 1028, SEQ ID NO: 1030, SEQ ID NO: 1032, SEQ ID NO: 1034, SEQ ID NO: 1036, SEQ ID NO: 1038, SEQ ID NO: 1040, SEQ ID NO: 1042, SEQ ID NO: 1044, SEQ ID NO: 1046, SEQ ID NO: 1048, SEQ ID NO: 1050, SEQ ID NO: 1052, SEQ ID NO: 1054, SEQ ID NO:

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1056, SEQ ID NO: 1058, SEQ ID NO: 1060, SEQ ID NO: 1062, SEQ ID NO: 1064, and complementary sequences thereof;

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- 15 x. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1262, SEQ ID NO: 1264, SEQ ID NO: 1266, SEQ ID NO: 1268, SEQ ID NO: 1270, SEQ ID NO: 1272, SEQ ID NO: 1274, SEQ ID NO: 1276, SEQ ID NO: 1278, SEQ ID NO: 1280, SEQ ID NO: 1282, SEQ ID NO: 1284, SEQ ID NO: 1286, SEQ ID NO: 1288, SEQ ID NO: 1290, SEQ ID NO: 1292, SEQ ID NO: 1294, 20 SEQ ID NO: 1296, SEQ ID NO: 1298, SEQ ID NO: 1300, SEQ ID NO: 1302, SEQ ID NO: 1304, SEQ ID NO: 1306, SEQ ID NO: 1308, SEQ ID NO: 1310, SEQ ID NO: 1312, SEQ ID NO: 1314, SEQ ID NO: 1316, SEQ ID NO: 1318, SEQ ID NO: 1320, SEQ ID NO: 1322, and complementary sequences thereof;
- 25 y. a nucleic acid molecule selected from the group consisting of NO: 1346, SEQ ID NO: 1348, SEQ ID NO: 1350, SEQ ID NO: 1352, SEQ ID NO: 1354, SEQ ID NO: 1356, SEQ ID NO: 1358, SEQ ID NO: 1360, SEQ ID NO: 1362, SEQ ID NO: 1364, SEQ ID NO: 1366, SEQ ID NO: 1368, SEQ ID NO: 1370, SEQ ID NO: 1372, SEQ ID NO: 1374, SEQ ID NO: 1376, and complementary sequences thereof;
- 30 z. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1390, SEQ ID NO: 1392, SEQ ID NO: 1394, and complementary sequences thereof;
- aa. SEQ ID NO: 1401, or the complementary sequence thereof;
- bb. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1418, SEQ ID NO: 1420, SEQ ID NO: 1422, SEQ ID NO: 1424, SEQ ID NO: 1426, and 35 complementary sequences thereof;

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cc. a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1435, SEQ ID NO: 1437, SEQ ID NO: 1439, and complementary sequences thereof; and,

dd. SEQ ID NO: 1446 or the complementary sequence thereof.

- 5      9. An isolated nucleic acid molecule, as claimed in Claim 5, wherein said nucleic acid molecule is less than about 5 kilobases in length.
- 10     10. An isolated nucleic acid molecule, as claimed in Claim 5, wherein said nucleic acid molecule is less than about 70 nucleotides in length.
- 10     11. A method of genotyping an individual comprising:
- a. obtaining a nucleic acid molecule sample from an individual;
- b. determining whether said nucleic acid molecule sample comprises a sequence of a nucleic acid molecule of Claim 5.
- 15     12. A method of genotyping an individual, as claimed in Claim 11, wherein said nucleic acid molecule sample is genomic DNA.
- 15     13. A method of genotyping an individual, as claimed in Claim 11, wherein said determining comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence and the corresponding wildtype sequence.
- 20     14. A method of genotyping an individual, as claimed in Claim 11, wherein said step of determining comprises amplifying a selected region of the nucleic acid molecule of the individual.

## SEQUENCE LISTING

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<120> Genetic Typing of Human Genes And Related Materials And Methods

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tcattgtttt tccttttttt ccatagttgc attaaaatcc tcccctactg aaagaaacgg      240
aggccaggat aactgtagag cagcaaattt cagagaaggc ctgaacttac aagaaggaga      300
attcttatta caggtaaatt ttagtaaata tagtttctta cactaaggac agttgtaaatt      360
ggaaaatgaa ttaataagtc ttttagtaat tccctgttta cttaggattt gctcaatggt      420
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caagggaagt taaagtatct tcatggacag aaaaagaaag ggaaagatgg atcaatactt      600
ccacctcagt tggcttttgt tgcgatagct actccacttc agccaccatc catacttgaa      660
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tgtgatgcca agtaagttag actttttcac ttttatttta ttggatgtac attatgtttc      780
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aaaatgtttg atagaattht tttctaagac tttttgtac acaatthtag agatgaggaa 180  
ggaacagagc atttacgaaa acgaaatacg aagttgcctt ttatgtttac cactggagaa 240  
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gaacagtgtc ttttagcatg atgaagcaga tgatgctgct ttttctatcc tttttcttac      180
tctttctttt cttccccctt ctctttgtat ttttccttat ctgtggcaag agaggacaag      240
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ttctttccat gcagggaaaa tcacagtga attgaacggc ggcgacggaa caagatgaca      180
gcctacatca cagaactgtc agatatggtg cccacctgta gtgccctggc tcgaaaacca      240
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tatagttctg agagagtctg gaatctgggt gaatctcttg aaagttttcg ttttttggac      420
aagaattcag cttttcagga agaagtcaga caatgggaaa acgaatttca gtccttggct      480
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gtttattgtc tcatgtgaga caggcagggg ggtgtatgtg tctgactccg tgactcctgt      180
tttgaaccag ccacagtctg aatggtttgg cagcacactc tatgatcagg tgcaccaga      240
tgatgtggat aaacttcgtg agcagctttc cacttcagaa aatgccctga caggtgagag      300
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tgttttagct gttaaattgg tttgttgact ctggcaaggc ttcaagaatt ttctacttta 420  
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gcgtatcctg gatctaaaga ctggaacagt gaaaaaggaa ggtcagcagt cttccatgag 180  
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tggattagct ccagtggatt aaatttaact ctccataccc agatggattg taacacagaa 360  
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ggaccagtt tctgtgaata ggctgagctt tgtgaggaac agatgcagggt gagatcctaa 180  
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tactgtagtc gttccttcag cagctctcac ttgcatccct tacctccac ttaacatccc 300  
ttacctcca cttacttttt ttctggcaat attttcttaa acttctaaaa cttctcttga 360  
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gcaggtaaga aagtgaaata gtaaatatatt ccccttggtta cagttgggttc ctcacagagt 180  
 ccatgaaagc taatatattat tatataacctg gtatatgaaa tgtacttttg tgtaagatga 240  
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 gctggccagg gaagcaagtt ttgcctagt ggcattggca gattgcaggc aagtatgaat 180  
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cagaattgga catggtacca ggaagagatg gactggccag ctacaatcat tcccagggtga 180  
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caacatcaat gcgggtatgt ttctttctca ttatcctttt aaattctcat ttagatcact 300  
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aactcctttt ggtccacaga tcagagtaaa ggcattctct ccagcactgt ccctgccacc 180  
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ggcctagcgt gaggcaaaca agctgctttt cttcctccta tttctttgca cctgtcctat 420  
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 ttgtcctttg attcctagct tctgtgataa atctatcctt ttaatctttt acctcattta 180  
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aggaagcatg cctggattga ggtgtttggt tgggggtata tgtgagaaga cagagagggga 420  
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gaatctaaag tttgtgatgc ttcacaacct ggagcattca atgggaatgc actcatcga 180  
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atattgcctg attctgtgga ctggagagag aaaggggtgtg ttactgaagt gaaatatcaa 240  
gtgagtatta ccatcccaag cctctgaacc ctaggtagag ctctttaaat gcttagtcta 300  
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<400> 439  
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<210> 440  
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<210> 442  
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<400> 444  
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<400> 465  
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cccagcgccg ccgccgcagt gggtcggggc ctcaggaggc agaccgcgct gggcttgcat 180  
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<210> 473  
<211> 618  
<212> DNA  
<213> Homo sapiens

<400> 473  
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gtttgcattt tccagttcct ggcagtatcc ctttctagtg gctgcttctc aatgaatatg    240
aacagtgtct gtttccatgt gctgccatga caaatccac agaatgttcc tgatgttctt    300
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aatagaaaac acccaccttt tctgtgaaga caaatgttgt ttaaatggta ttaatgggag    540
tattgcagtc accttaaaac atacttgcta atatattgtg gcaaatggtg aacgaaaact    600
gtgatgaaac tattggga                                618

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<210> 474
<211> 500
<212> DNA
<213> Homo sapiens

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ctcatggaag aaaactgcag gaagtgtcc gagaccgcta aagtctgcct cccaagaat    180
ttctccataa aagaaatctt tgacaaggcg atttcagcca gaaagatcaa ccgccccatg    240
ctccaggcag ctctcatgct caggaagaaa ggtaaggatc tgatactggc caatctcagg    300
ccgaaccacc cagaaccctc gggagcatta ggtcagaatc cattgaagtg agctttgaga    360
tcacagatct tctgagccac gatggaaagc ctctttaaac atggcccca agcaagtttt    420
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aaagcaattg atgcccatga                                500

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<211> 627
<212> DNA
<213> Homo sapiens

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<222> (372) .. (372)
<223> n = a, c, g, or t

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gatctagaaa gttctcccag aggtgggcat ttggctccat tgtatagctc ttacagaact 540  
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<213> Homo sapiens

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gcccctgttt gcattctggg gagtttcttt ctgagattct cccatgctgt tttgggctca 180  
ggtcgttttt ttggatgaca tcggggctaa tctgaagcca gcccgtagact tgggaatggg 240  
caccatcctg gtccaggaca ctgacacggc cctgaaagaa ctggagaaag tgaccggaat 300  
ccaggttaact tgacttctga gcgagccaag cttcctggac tcatctgtgg tttctggact 360  
caggagaaaa ccacgagcag agaagctgct gtccgaggag tccatgaatg actcctgggc 420  
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ttgcctcttt ctctgcagtc 500

<210> 477  
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<212> DNA  
<213> Homo sapiens

<400> 477  
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aaaaggatgat ttccaaggcc tcccctggca ccagtattca ggagagcctc tcacggaagg 180  
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cctctgccga cctcttgcaa tccaagtgaac atgagccatg ggtacgtgac agtaaaggatg 300  
agtcagtttt gtctctcagt cggctaagtg ctctcccacc aggtcaccta aaacgaccag 360  
cagagacacc caagaggctg agctgtgagg atcacctgaa cctgagcctg ggaagtggag 420  
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tctcaagaaa aaaaaaaaaa aaaa 504

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<211> 959  
<212> DNA  
<213> Homo sapiens

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cagggtccgt ctgcattttg tggagctggg ctccggccct gctgtgtgcc tctgccatgg 180  
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<211> 491  
<212> DNA

<213> Homo sapiens

<400> 479

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aaatatgttt cttttatttt taattgcaga aatagaagaa tattgcatgg aagtgttatg      240
taaggtaaga agaatcttgg gtaacatctt ccccatcctg cgatttttgt tgctataaac      300
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aatcctact gaaagttgaa cagtatttcc aaatgatagc ccacatgtat gcagcatcga      420
ctgtgtgtca ggtcttcctc caagcaactg acagaagaga aaactgagtc atgggaagtt      480
aaaggttaatt g                                                    491
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<210> 480

<211> 290

<212> DNA

<213> Homo sapiens

<400> 480

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acagcagttt tggggaggac gcagttcagc ccatcataaa ggctgaggca ggcgggtgtg      180
gttgctgatt ttgctgtgt gtgtcttctt ccttaggaga tggtaacctt cctggataaa      240
ctggtaagtc attattttga actgatatct ttggagaatt cctttggggc          290
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<210> 481

<211> 489

<212> DNA

<213> Homo sapiens

<400> 481

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ccctgggtgc gaggggctgg ctgatggccg aacctctcag caccctgttc cagaagcctc      180
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gtaattgggc ctcgggcaat aaagatttgg aggaggctgg acttgaactc ctgtgagaat      360
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tgctcctcag atctttaagc ccagaaaact tctcaaaaac aagtaggtag tctgggaagg 420  
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<212> DNA  
<213> Homo sapiens

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&lt;210&gt; 486

&lt;211&gt; 1130

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 486

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<400> 1201  
agtgatggga aaagggcaga g 21

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aggcaccttc aaggatcatc gctgaagaag atagcagctc cacaggtcaa ggcgatcttc 180  
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cagggtcag ggggctgca ctcctagggg cttgcagact agtgggagag aaagaacatc 300  
gcagcagcca ggcagaacca ggacaggtga ggtgcaggct ggctttcctc tcgcagcgcg 360  
gtgtggagtc ctgtcctgcc tcagggtttt tcggagcctg gatactcaag gaacaagtag 420

acctggccgc ggggagtgagg gagggaaggg gtgtctattg ggcaacaggg cggggcaaaag 480  
ccctgaataa aggggagcag ggcaggcgca agtggcagag ccttcgtttg ccaagtcgcc 540  
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gctgcataaa gagagactcc cccatccagt gtatccaggc cattgcgggtg agtcaatgcc 180  
gggtgttggg tgggaccaag ctgaatggaa gggagagaga aatggaaaaa gatagaacac 240  
gagctctcct tacttcctct gcttcacctg ttgggcaacg aagtggggag ccgtcctctc 300  
tcacaggga ctttgc 316

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gttctgcctg gggacccaga ggccacgggt gcctcagcct gtgccctgag ctgtgtggat 300  
taagactggg ggaacatgtg gaggtggagt ctgggtcaca tcacacatgt agggaatgga 360  
gtcgtgaggc tctgggcccag atgaaggccg ttcctcctga cgctgaccca cgagaggagg 420  
acacacgtga gctgtgagga aactgcagca cagcattccc cctcccaccg gagacttttc 480  
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tataggaaca cttcgtccat tcttgaattg gacgggtcca cctgagccca ttgaggcagg 720  
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gccagggcta ctgttcaca gggaggggct ggggagggct gcctgtgctt acccctgatg     180
gtttctcttt tcacaggtgt ctgagagacg gggctggaga cgtggctttt atcagagaga     240
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tagactccct ccacctcac cttccctgca gaggacctgt cagacgaggc tgaaaggagc     180
gagtatgagt tactctgccc agacaacact cggaagccag tggacaagt caaagactgc     240
catctggccc gggtccttc tcatgccgtt gtggcacgaa gtgtgaatgg caaggaggat     300

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gccatctgga atcttctccg ccaggcacag gtatcttcac ccacggctct cccacttgc 360  
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tctgtagct ttgctgcagg atagcac 447

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gaaaagtttg gaaaggacaa gtcaccgaaa ttccagctct ttggctcccc tagtgggcag 240  
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tgagcccagg agggctctga ggtccgcctg gtgtggctct ctacttccca gcagggtggc 420  
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<210> 1208  
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<212> DNA  
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gtgggcgagc aggagctgcg caagtgtaac cagtggagtg gcttgagcga aggcagcgtg 180  
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gaagtcaaca gtcaaagagg ccacgggggc ccgggtgagg cagggatgcc tggagaggtg 360  
tgctcagggc cagaaagcat tttagtttca aaaagcagtt tactgtggg 409

<210> 1209  
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<212> DNA  
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<400> 1209



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gggagtgagg ctatgagtaa tccattcgg tgaatgcagg tgaaacatta tgatgaacag      360
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<212> DNA
<213> Homo sapiens

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gcattagcca ctttcagggt caaggataag ttcttgttgc tggaagagga agtggcagga      300
actgtaaaaa aaacagaaag aattgcagcc ctagaagcta tagggcttct aggagcaata      360
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atatcttgct gtggcgggtg ttaggagatc agacactagc cttacctgga actctgtgaa      180
aggcaagaag tcctgccaca ccgccgtgga caggactgca ggctggaata tcccatggg      240
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gtgggccacc ctggagggtg ggcattattgt gctgtggaac cttaggaag ggagggagg      360
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ttgcttgtgt ggactcaggt ttgaagagct gactccccgt gttccttctc tccagatgaa 180  
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tacactgggg ctttcgggtg agtctgtgac tgagctccat caggatgggg ccttacctca 360  
tccctcagca tgtcagcatt gcagttctaa ggagccagat gtgacctgtc acagcagagt 420  
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atgtttactt ccatatttca gtttttgga tgcattatc aaatatttat gaaagcccca 180  
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tcgatggcaa acggaagcct gtgactgagg ctagaagctg ccatcttgcc atggccccga 240  
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aacaggatatg gaccacaggg cttctagtgc tttcttagct gtgtgggctc atgttaggtg 360  
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